JAMES YOUNG SIMPSON

1811—1870

From a daguerreotype in the collection of Professor James Young

Endocrine Allergy
Clinical Reactions of Allergy to Endogenous Hormones and their Treatment*

BY

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IN a previous paper (Zondek and Bromberg, 1945) it was reported that a state of hypersensitivity to endogenous hormones exists in certain individuals. A hypersensitive state has been observed both in respect to protein-like, e.g., insulin and pituitary secretions, and to steroid hormones. The term "endocrine allergy" covers the various manifestations of the condition of hypersensitivity to the endogenous products of the endocrine glands. Since allergy is elicited generally only by body-foreign substances, it is surprising to find that it can exist also in respect to an endogenous secretion. The following clinical and experimental findings seem, however, definitely to establish the occurrence of this condition in man.

A. EXISTENCE OF ENDOCRINE ALLERGY.

1. Allergic hypersensivity to the steroid hormones (oestradiol, progesterone, testosterone and corticosterone[1]) or to the products of their metabolism which are excreted in the urine (oestrone, pregnandiol, androsterone) can be demonstrated in certain pathological conditions generally related to menstruation or to menopause by means of active cutaneous tests. Reactions of this type have also been observed with insulin and gonadotropin. The positive cutaneous reaction appears in such cases 24 to 48 hours after the intracutaneous injection of oily solutions or aqueous suspensions of the allergenic steroid hormone. It persists for 24 to 48 hours or

[1] Throughout this paper desoxycorticosterone acetate was used for the detection of corticosterone sensitivity.

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more. The specific character of the manifestation is reflected in the specificity of the skin reaction.

2. The positive local reaction originally elicited by an intracutaneous injection of a steroid hormone can recur at its first site when the allergen is injected subcutaneously at a second site. This phenomenon, called by us the "recurrent reaction", shows that the injection hormone is an authentic allergen.

3. Some patients, in whom the symptoms of allergy recur in the premenstruum, may show a recurrent positive cutaneous reaction in the same phase in several successive menstrual cycles. It seems significant that this "retarded cutaneous reaction" recurs at a time point which coincides with the attainment of peak hormone concentrations in the body. This circumstance further strengthens the proof of the existence of endocrine allergy.

4. Allergic patients not previously treated with hormones can sometimes react to an injection of even minimal amounts of a steroid hormone with serious general symptoms of an allergic nature, such as asthma, urticaria, angioneurotic oedema, fever, etc.

5. In one case, a severe attack of pruritus vulvae has been observed following the ingestion of 50 g. of glucose by a patient in climacterium suffering from pruritus vulvae· Diabetes was not present in this patient. On the contrary, her blood analysis and a sugar tolerance test revealed hypoglycaemia due to hyperinsulinism. Following an intradermal injection of a minimal dose of insulin (0.0002 I.U.) a typical positive cutaneous reaction to this hormone was obtained. Local as well as general methods of treatment (including hormones: oestrogenic hormones and testosterone) failed to give relief. Desensitization treatment with insulin procured relief.

6. The presence of reagins to a hormone can be demonstrated in certain cases by means of passive transfer tests with serum taken from women hypersensitive to endogenous sex hormones and injected intracutaneously into normal women, followed by injection of the allergen at the same place (Prausnitz-Kuestner test).

7. Serum from patients sensitive to oestrone or oestradiol elicited in normal women a positive cutaneous test ("endogenous passive transfer test") when it was injected during their premenstrual phase. This fact shows that skin reactions which become positive when the allergic hormone in the body reaches its peak value can be elicited by serum reagins.

8. The properties of the hormone reagins resemble those of ordinary reagins (Zondek and Bromberg, 1945).

9. Allergic constitutional or hereditary predispositions are often disclosed by the personal and familial histories of patients with a positive cutaneous reaction to a hormone.

10. Often desensitization with an allergenic hormone brings complete relief. The results obtained suggest that the desensitization treatment is specific.

The view has been put forward that migraine in women with allergic tendencies may be due to the fact that they have an exaggerated susceptibility to pituitary gonadotrophin (Glass, 1936). Geber (1939) and Urbach (1939) found that serum taken from patients during an attack of premenstrual dermatitis is able to elicit severe skin reactions when it is injected into the skin of the same patients. Allergic hypersensitivity to insulin has been demonstrated in skin tests with injections of crystalline animal insulin and human insulin (Lowell, 1942) and also in positive transfer tests (Prausnitz-Kuestner test) with serum containing reagins to insulin (Tufts, 1928).

Allergy to progesterone has been assumed in cases of hyperemesis of pregnancy (Finch, 1938).[2]

The positive intracutaneous test to steroid hormones was found to be relatively frequent in cases of complaints connected with menstruation or menopause. It was this observation which led us to suspect the existence of sensitivity to endogenous hormones in cases of this type. Patients suffering from manifestations of an allergic nature, such as asthma, vasomotor rhinitis, angioneurotic oedema, urticaria, migraine, and certain forms of eczema related to menstruation or menopause, often gave positive skin reactions to different steroid hormones. Hypersensitivity to hormones was also found in patients with manifestations strictly linked to menstruation or menopause, e.g., premenstrual tension, premenstrual fever, vomiting or nausea, pruritis vulvae and certain ocular disturbances (superficial keratitis and chronic recurrent conjunctivitis).

The present communication deals with certain clinical features of the condition of endocrine allergy and describes the methods which we employ in this condition in order to bring about desensitization.

Our material: 216 women were tested[3] in regard to sensitivity to hormones. Of them 32 were in good health and had regular periods, 68 suffered from disturbances not connected with the genital function, and 116 had complaints related to menstruation or menopause. A positive skin reaction to hormones was never observed in healthy women. Only 2 of the 68 cases (3.3 per cent) with complaints not related to menstruation or menopause showed positive responses. In patients with complaints related to menstruation or menopause, a positive cutaneous test to a hormonal allergen was found in 73 cases (63 per cent) (Table I). Endocrine allergy tests were only undertaken after trials of ordinary exogenous allergens and miscellaneous trials of different routine methods of treatment proved unsuccessful. The majority of 73 patients who proved sensitive to an endogenous hormone have a familial or personal history of allergy and the blood picture showed marked eosinophilia. In several cases specific desensitization was carried out. The cases which showed a positive cutaneous test had the following complaints:

(a) In relation to menstruation: 2 asthma, 2 vasomotor-rhinitis, 3 angioneurotic oedema, 4 urticaria, 1 eczema, 4 acne, 6 migraine, 3 superficial keratitis, 22 premenstrual tension, 3 premenstrual fever, 10 pruritus vulvae.

(b) In relation to menopause: 1 asthma, 1 urticaria, 1 eczema, 3 migraine, 5 pruritus vulvae.

The observed cases, as has already been mentioned, had one feature in common: the complaints related to menstruation or menopause. This leads us to consider that hormones or their derivatives in certain cases sensitize the organism only when their concentrations in the body tissues are at the peak level, e.g., towards the termination of the menstrual cycle or at the beginning of the menopause (first hyperhormonal phase) (Zondek, 1931; 1935a).

Steroid hormones (oestrone, oestradiol, progesterone, pregnandiol, testosterone, androsterone and corticosterone) as well as prolan (chorionic gonadotrophin) and insulin have been found capable of allergenic activity. The clinical manifestation of endocrine allergy can be the same although the hormonal allergen which is operative in different cases may vary.

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[2] In a series of 12 women suffering from vomiting of pregnancy we were unable to find positive skin reaction to steroid hormones.

[3] In our previous paper (Zondek and Bromberg, 1945) we reported 165 cases. In the meantime 51 additional women were tested.

TABLE I.

Distribution of Cases Tested for Endocrine Allergic Condition.

Diseases investigated		Related to menstruation			Related to menopause		
		Number of cases tested	No. of hormone sensitive cases	Hormonal allergen	Number of cases tested	No. of hormone sensitive cases	Hormonal allergen
Respiratory system	Asthma	2	2	1 oestrone 1 corticosterone*	3	1	Oestrone
	Vasomotor rhinitis	2	2	1 oestradiol 1 testosterone	–	–	
Cutaneous system	Angioneurotic oedema	6	3	1 progesterone 2 testosterone	–	–	
	Chronic urticaria	8	4	2 oestrone 1 progesterone 1 testosterone	3	1	Corticosterone*
	Chronic eczema	4	1	oestradiol	2	1	Testosterone
	Acne	10	4	3 oestrone 1 corticosterone*	–	–	
Nervous system	Migraine	11	8	2 oestradiol 2 oestrone 1 progesterone 1 pregnandiol 1 androsterone 1 corticosterone*	6	3	1 oestrone 1 testosterone 1 prolan
Ocular system	Superficial keratitis	3	3	2 corticosterone* 1 androsterone	–	–	
Genital system	Premenstrual tension	33	22	4 oestradiol 7 oestrone 1 progesterone 5 testosterone 1 androsterone 4 corticosterone*			
Genital system	Pruritus vulvae	13	10	1 oestradiol 4 oestrone 2 progesterone 1 corticosterone* 2 testosterone	7	5	2 oestrone 1 prolan 2 insulin
	Premenstrual fever	3	3	1 oestrone 2 testosterone	–	–	

* Desoxycorticosterone acetate served as test substance.

B. DIAGNOSIS OF ENDOCRINE ALLERGY BY CUTANEOUS TESTS WITH HORMONES.

Allergenic Hormones. The methods used to detect allergenic hormones have been presented in an earlier paper (Zondek and Bromberg, 1945). The following hormones and their metabolites of the genital and adrenal glands were tested: 1, oestradiol; 2, oestrone; 3, progesterone; 4, pregnandiol; 5, testosterone; 6, androsterone; 7, desoxycorticosterone acetate. Solutions of the steroids were prepared in oil in concentrations of 0.1 mg. per 0.1 ml. pure olive oil. Recrystallized steroid hormones were used. The olive oil was first purified

according to the Pharmacopeia Helvetica VI, and heated at 100°C for 48 hours. The hormone crystals were dissolved in this oil at 100°C. by heating for another 24 hours. In this way sterile, clear, homogeneous solutions must be obtained. Control tests were performed on the oil vehicle and on cholesterol alone. The hormone and the control solutions were applied intradermally with a small needle. Originally the dose employed amounted to 0.1 ml. containing 0.1 mg. of the crystalline hormone. The injections were made on the outer border line between the volar and dorsal surfaces of the arm and forearm. This site is preferable to the more commonly used volar surface, the skin on the latter being too thin for an injection of oil. In order to avoid immediate non-specific oil reactions, the needle should be inserted through the epidermis into a layer somewhat deeper than that usually employed in tests of aqueous solutions.[4] To avoid contamination, a separate syringe and needle is used for each test. The skin reaction was read 24, 48 and 72 hours after the injection. A reaction was considered positive when 24, 48 or 72 hours after injection a red or rose-coloured, slightly elevated papule, at least 0.5 cm. in diameter, appeared at the site of injection. The reaction was also considered positive when 24 or 48 hours after the injection a pink erythema, 2–3 cm. in diameter, appeared at the site of the injection. Positive reactions persist generally for 48 hours, but sometimes remain as a rosy, itching erythema for many weeks. When the 24 hours' reaction is of an inconclusive nature, a second reading can be taken at 48 hours. Specific positive reactions persist usually for 48 hours and sometimes for 72 hours.

Cases in which an intracutaneous injection of 0.1 mg. of steroid hormone produced an unusually severe local reaction were tested in respect to graded dilutions of the allergen. In some instances 0.001 mg.

(1 gamma) sufficed to bring about a local reaction.[5]

In certain cases a positive reaction appeared 3–5 hours after the injection and disappeared some hours later. Such results were read as doubtful, since prolonged contact between an allergen and a tissue is a characteristic of a true allergy reaction. In doubtful cases the following test was also performed: 24 hours after an intracutaneous injection of 0.1 mg. of the test hormone, 1 mg. of the latter was injected subcutaneously at a new site. The patient was reported as sensitive if 3–5 hours after the second injection a slight reddening accompanied by itching appeared at the site of the first, the intradermal, injection ("recurrent test reaction"). Since reactions are usually read 48 or 72 hours as well as 24 hours after the injection, we employ the recurrent test reaction now only in exceptional cases.

In rare cases reactions became positive shortly before a menstrual flow, 2–3 weeks after an injection. Reactions of this kind were reported as positive ("retarded reaction"). In some cases positive cutaneous reactions recurred spontaneously in the premenstrual period of several successive cycles ("periodic retarded reaction"). In one case of migraine with sensitivity to oestrone, the positive skin reaction recurred in every one of 8 subsequent premenstrual periods, after which, pregnancy interven-

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[4] Consequently there does not appear a wheel at the site of injection but a slight elevation of the epidermis. We have learned that this point is of decisive importance, otherwise non-specific reactions may occur.

[5] In recent months, we employed for the tests a solution of 0.01 mg. hormone in 0.1 ml. oil. This amount elicits a positive skin reaction in a majority of allergy cases. It is possible, however, that it fails to elicit a positive reaction in a certain percentage of them. Our experience on this point remains at present inadequate for any definite conclusion.

ing, both the positive skin reaction and the clinical complaints disappeared.

Sensitivity to oil (7.5 per cent) or cholesterol (1.9 per cent) alone was observed in 9.4 per cent of the cases. These were excluded from further investigations. When sterile solutions are used, the intracutaneous injections never evoke an inflammatory reaction. Questions which colleagues have addressed to us lead us to believe that certain points in our earlier description (Zondek and Bromberg, 1945) of the technique have been misunderstood. Errors have arisen in consequence. The quality of the oil vehicle is a very important point. We use olive oil made from Palestinian olives, and purified as prescribed in the Pharmacopeia Helvetica. The hormone preparations should be of the highest purity and recrystallized. Contaminants can frequently elicit non-specific reactions. To check this possibility we first test our preparations on healthy subjects. Normal individuals should give no positive skin reactions to hormonal allergens.

For the cutaneous test of gonadotrophin (korotrin) or insulin, aqueous solutions were used. Such tests were read as positive when a large erythema with urticarial oedema and itching appeared at the site of the injection 1–2 hours after the inoculation. The insulin was in a dilution of 1:10,000 (0.1 ml. = 0.0002 I.U.) and the korotrin (prolan) was dissolved in normal saline (1 ml. = 1 I.U.); control tests for prolan were run on the same solution after inactivation of the gonadotrophin by boiling.

PRINCIPLES OF CUTANEOUS TESTING WITH STEROID HORMONES.

As has been shown above, the clinical diagnosis of endocrine allergy is essentially based on the positive cutaneous tests for hormonal substances. Since the specifity of the positive reactions is greatly dependent (as in other allergic tests) on accurate technique, the principles of cutaneous testing with steroid hormones will again be summarily reported.

Materials: (1) Olive oil (purest quality available) purified according to Pharm. Helvet. VI, and heated at 100°C for 48 hours.
(2) Recrystallized steroid hormones (oestradiol, oestrone, progesterone, pregnandiol, testosterone, androsterone, desoxycorticosterone acetate).
(3) Cholesterol.
(4) Nine syringes 1 ml. (preferably tuberculin syringes).
(5) Fine needles for intracutaneous testing.

Preparation of Test Solutions. The hormones as well as cholesterol are dissolved in oil by heating at 100°C. for another 24 hours until a sterile, clear, and homogenous solution is obtained. All the substances are used in concentrations of 1 mg. in 1 ml. of oil.

Site of injection. Outer border line between the volar and dorsal surfaces of the arm and forearm. Injections must be given into a skin layer deeper than that into which aqueous solutions are injected.

The positive reaction (readings: 24, 48 and 72 hours after the injection). Red or rose-coloured · slightly elevated papule at least 0.5 cm. in diameter, or pink erythema 2–3 cm. in diameter.

All other reactions reported above ("recurrent reaction", "retarded reaction" and "periodic retarded reaction") were employed only as contributory methods serving to confirm the allergy to endogenous steroid hormones and not as usual tests for diagnosis of endocrine allergy.

The significance of positive cutaneous reactions for hormones.

The positive skin reactions to steroid hormones are of "delayed" type, since

they commonly appear or reach their maximum intensity 24 hours after injection. On the other hand, the water-soluble hormones yield reactions of "immediate" type, appearing in 1–2 hours after injection. It has been assumed that both reactions result from the same immunological process (Dienes, 1931: Simon and Rackemann, 1934: Jones and Mote, 1934).

It has also been assumed that "delayed" skin reactions appear only when the body has been exposed to the action of the allergen for a long period of time (Vaughan, 1929), which is also generally the case in endocrine allergy, or that they indicate the formation not of circulating, but of cellular antibodies (Urbach, 1943).

C. CLINICAL OBSERVATIONS.

With few exceptions, the existence of a condition of allergy to endogenous hormones deserves consideration in cases of disorders connected with menstruation or menopause. In certain conditions, endocrine secretions which are harmless to the great majority of normal individuals may elicit in different organs allergic reactions, such as asthma in the bronchial system, or urticaria on the skin. A particular organ can also react with the same allergic symptoms to different hormones. Urticaria, for example, can be the result equally of a state of hypersensitivity to either oestrone, testosterone or progesterone.

Endocrine allergy can frequently play a role in gynaecological conditions which are associated with the premenstrual phase, e.g. hypogastric pains, migraine, vomiting, and fever. Pruritus vulvae related to menstruation or menopause is often due to endocrine allergy.

In the following, the allergic reactions to endogenous hormones are classified according to the organ affected. The case reports will include both an account of the symptoms and a brief mention of the results obtained in desensitization.

D. ENDOCRINE ALLERGIC REACTIONS OF THE DIFFERENT SYSTEMS.

RESPIRATORY SYSTEM.

(a) *Asthma related to menstruation or menopause.*

In some women with asthma there is evidence of a relationship between the clinical course of the disease and genital function. The onset of asthma is frequently associated with the first menstruation at puberty. The attacks, moreover, often recur at a given point in the menstrual cycle; generally they are experienced in the premenstrual period when the steroid hormones reach peak values in the body. Often pregnancy brings improvement or relief from the asthmatic attacks. Often onset of asthma occurs during the hyperhormonal early phase of the menopause. It has been mentioned that certain cases of asthma may be due to the presence of a hypersensitivity to oestrogenic hormone (Urbach, 1943).

Five cases of asthma were studied. In 2 the attacks always recurred before menstruation. In 3 cases asthma related to onset of menopause. Both of the 2 premenstrual cases exhibited hormone sensitivity, 1 to oestrone and the other to corticosterone. Desensitizing treatment was followed in the oestrone-sensitive case by recovery and in the corticosterone-sensitive woman by improvement. Only 1 of the 3 menopausal cases exhibited hormone sensitivity. In this case, one of oestrone-sensitivity, desensitization produced marked but transient relief. Two cases of asthma are reported fully below.

CASE 1. Mrs. R.M. 33 years old. According to the family history, patient's mother complained of asthma, and 2 of her brothers suffered from hayfever. Eosinophilia, 3 per cent. Slight lymphocytosis, 38 per cent. For about 5 years asthmatic fits had recurred regularly in the 10 days preceding menstruation. In the last pregnancy, 2 years bef——

the complaints disappeared during the second half of the pregnancy, after some aggravation during the first months. A cutaneous hormone test, performed after menstruation, revealed the existence of a sensitivity to oestrone. Twenty-four hours after the test, for the first time after a menstruation, a serious asthmatic attack occurred. Desensitization treatment with gradually increasing daily doses of oestrone (from 0.001 mg. to 1 mg.), administered subcutaneously in a series of 30 injections, was undertaken. In an observation period of 5 months following the treatment, the patient was free from asthmatic attacks. At the end of this time the patient stopped coming for observation.

CASE 2. Mrs. H.P. 52 years old. Suffered in the last 2 years from frequent and severe attacks of asthma. Tests for external allergens gave negative results. The asthmatic fits in the form of severe daily attacks began simultaneously with the menopause. Hormone tests revealed sensitivity to oestrone. Treatment with subcutaneous injections of gradually increasing doses of oestrone was instituted. After the injections, the patient remained free from asthmatic attacks for 3 months, after which an asthmatic attack occurred. The patient then received a second series of oestrone injections, and for 2 months no attacks occurred. After a third course of treatment, no asthmatic attack was reported during a follow-up period of 1 year.

(b) Vasomotor rhinitis in the premenstrual period.

Vasomotor rhinitis, characterized by paroxysmal attacks of sneezing accompanied by nasal obstruction or serous rhinorrhoea, is generally due to exogenous, chemical or bacterial allergens. However, in some instances, the relationship between the clinical picture and the hormonal cycle suggests that female sex hormones are the allergenic substances. Some women have the attacks periodically in connexion with menstruation; moreover, pregnancy sometimes improves the rhinitis.

Selected cases with hypersensitivity to hormones—one to oestradiol, and the other to testosterone—were studied. Specific desensitization proved successful in both

cases. In the same context a case reported by Riebel (1935), in which attacks of premenstrual rhinitis were related to hypersensitivity to oestrone, should be cited. The case with vasomotor rhinitis due to hypersensitivity to oestradiol is reported below.

CASE 3. Mrs. P.M. Age 37. Had been suffering from attacks of vasomotor rhinitis for the last 3 years.[6] All tests of external allergens were negative in result. Paroxysms of rhinitis always occurred in patient during the week preceding menstruation. Paroxysms were characterized by violent sneezing accompanied by an irritating mucous discharge and severe photophobia. During the same period, patient also suffered from urticaria, headaches and heavy spasmodic pains in the lower abdomen. Onset of menstrual flow always produced complete relief from all these symptoms. The family history revealed asthma in patient's mother and sister. Blood eosinophilia, 7 per cent. Cutaneous hormone tests revealed a sensitivity to oestradiol. Desensitization treatment was performed by subcutaneous injection of oestradiol in increasing doses. Following this treatment, 8 premenstrual periods passed without pathological symptoms. Slight rhinitis before the ninth menstruation was treated by desensitization to oestradiol. During the 6 months which have since elapsed, the symptoms have not recurred.

ENDOCRINE ALLERGIC REACTIONS OF THE CUTANEOUS SYSTEM.

(a) Angioneurotic oedema. Although angioneurotic oedema is not always conditioned by allergic sensitization, there are numerous cases of this disease which have definitely been proved to be of allergic origin. Sudden attacks of pale, circumscribed swellings on various parts of the body occasionally occur in relation to the menstrual cycle and may be due to endocrine allergy.

Of 6 cases of angioneurotic oedema related to menstruation, 3 showed positive cutaneous tests to hormones, 1 of them to

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[6] We are indebted to Dr. Lachman, head of the Otolaryngological Department, for this case.

progesterone and 2 to testosterone. In all 3 positive cases, oedema of the face and of the skin of the hands and swelling of the mucous membrane of the lips and tongue were observed. The manifestations appeared 2–5 days before menstruation and persisted till the onset of the flow. In 1 case very severe headache and slight urticaria accompanied the symptoms. The 2 cases in which testosterone sensitivity had been detected were treated successfully by desensitization.

CASE 4. Mrs. C.R. Age 28. Married and mother of 2 children. In the last 4 years the patient had complained of paroxysmal swellings of the face, lips and tongue. The symptoms appeared regularly 2 days before menstruation and subsided following the onset of menstrual bleeding. Suffered also from severe headaches and slight urticaria. No contributory information was found in the family history. Blood picture: normal. Hormonal tests showed sensitivity to testosterone. Urticaria and slight oedema of lips developed following the performance of the tests. Desensitization with gradually increasing doses of testosterone was undertaken. Following treatment, the patient remained free from the mentioned disturbances for 2 premenstrual periods. The patient came back to us in her third premenstrual period with an attack of facial oedema and dyspnoea due to laryngeal oedema. The desensitization treatment was repeated and in its termination a 10 mg. pellet of testosterone was implanted. In the following 8 months no recurrences of angioneurotic oedema were observed. After this period the patient stopped coming for examination.

(b) *Chronic urticaria.* The variety of the aetiological factors and the short duration of urticaria render particularly complicated the study of its pathogenesis and therapeutic possibilities. All the cases examined by us involved complaints which had lasted for at least one year. Earlier attempts at treatment and investigations of the aetiology of the condition had been negative.

Eight cases of urticaria with exacerbation before and during menstruation were tested for hormonal sensitivity. Four of the cases proved to be sensitive to various hormones (2 to oestrone, 1 to testosterone, and 1 to progesterone). One of 3 cases of urticaria occurring at the onset of menopause showed a positive hormone cutaneous test (corticosterone). Desensitization treatment in the 2 oestrone-sensitive cases, in the progesterone-sensitive and in the corticosterone-sensitive cases gave satisfactory results. Recovery in the oestrone and in the corticosterone cases and improvement in the 2 other cases were reported.

CASE 5. Miss L.O. 25 years old. Regular menstruation. In the last 2 years the patient complained of attacks of urticaria occurring in the second half of the menstrual cycle. At onset of menstruation complete relief was always obtained. Search for an external or dietary allergic substance yielded negative results. Family and personal history without special findings. Blood eosinophilia, 6 per cent. The hormonal cutaneous tests revealed a sensitivity to oestrone. Specific desentization produced complete relief from the urticaria. The patient received 30 injections over a period of 1 month, the initial dose of 0.01 mg. being increased stepwise to 1 mg. per injection. Three years after treatment, the patient was still free from any of the symptoms.

(c) *Chronic eczema.* Endocrine allergy is very rarely a causative factor in chronic eczema. A relationship between hormonal metabolism and the clinical course of eczema may, however, occasionally be observed. In certain cases, eczema recurs at each menstrual period and disappears during pregnancy or at the menopause; in other cases the complaints seem to be related to the beginning of menopause. Hormonal hypersensitivity was found to exist in 1 of 4 cases of chronic eczema related to menstruation and in 1 of 2 cases of eczema related to menopause. The case in which the aggravation of the symptoms recurred at menstruation showed oestradiol sensitivity; that with symptoms in the menopause showed testosterone sensitivity.

Desensitization was carried out only in the last case, and without result.

(d) *Acne.* Ten cases of acne, with exacerbations 1 or 2 weeks preceding menstruation, were studied for hormonal sensitivity. Four cases showed a positive cutaneous test, 3 to oestrone and 1 to corticosterone. Desensitization treatment was practised in 3 cases with the following results: marked improvement of 1 oestrone-sensitive and of 1 corticosterone-sensitive case; no significant effect in 1 oestrone-sensitive case.

CASE 6. Mrs. R.Y. Aged 19. Suffers from severe facial or thoracic acne which is aggravated before each menstruation. Intracutaneous tests with hormones revealed sensitivity to oestrone. Cutaneous reaction remained positive after the inoculation for 10 days. Desensitization was *via* 2 routes: the percutaneous and the subcutaneous. For 3 weeks the patient received oestrone in doses of 1 mg. in lanolin by daily inunctions of the affected skin site and in increasing doses from 0.01 to 1 mg. by subcutaneous injection. Improvement followed this treatment, which was further extended by the implantation of 25 mg. of oestrone in the form of a pellet. There was still no relapse of the facial or thoracic acne 6 months after the treatment, when the patient was last seen.

ENDOCRINE ALLERGIC REACTIONS OF THE NERVOUS SYSTEM.

Various neurologic and psychic disturbances become aggravated during the menstrual period or at menopause. Manifestations attributed to diseases of the central nervous system (migraine, epilepsy) as well as to peripheral nerves (certain forms of neuralgia) may appear, become aggravated, or recur in relation to the genital function. Three cases of epilepsy[7] with fits coming on shortly before menstruation; 2 cases of premenstrual sciatica, 1 case of climacteric arthralgia of the knee, and 5 cases of premenstrual depressions, gave negative skin tests to hormones. On the other hand, migraine related to menstruation or menopause was found to be of endocrine allergic origin in a considerable percentage of cases.

Migraine. Attacks of migraine in women are often connected with the sexual cycle. The frequent onset of pains shortly before menstruation or at the beginning of the menopause and their relief or improvement during pregnancy suggest that there is a relationship between this syndrome and the endocrine secretions. Eight out of 11 cases of migraine related to menstruation showed sensitivity to hormones (2 to oestrone, 2 to oestradiol, 1 to progesterone, 1 to pregnandiol, 1 to androsterone, and 1 to corticosterone). In 6 other menopause cases, 3 had positive cutaneous tests, 1 to testosterone, 1 to oestrone, and 1 to prolan. Treatment was given in 8 cases, of which 6 showed either recovery or improvement.

CASE 7. Mrs. T.L. Aged 34. Married and mother of a 3-year-old child. Had been suffering for 7 years regularly on the 14th and 28th days of the cycle from migraine, which prevented her from pursuing her usual occupation. No organic cause was disclosed by various examinations. The blood picture showed high eosinophilia (12 per cent) and 40 per cent lymphocytosis. During her one pregnancy the patient had been completely free from headache. In the family records allergic diseases (asthma, urticaria, and hay-fever) were frequent. The cutaneous hormone tests disclosed a sensitivity to oestradiol. A positive intracutaneous test was elicited not only by the usual dosage of 0.1 mg. but even by as little as 0.001 mg. of oestradiol. Of interest is the fact that the local test, once induced, recurred spontaneously in the premenstrual phase of seven successive menstrual periods (" periodic retarded reaction "). 0.1 ml. of the serum of this patient, taken during an attack, was injected intracutaneously into the skin of a normal individual. The latter showed after 24 hours a positive skin reaction when 0.1 ml. of an aqueous solution of oestradiol (100 I.U.,

[7] Several cases of epilepsy occurring during the premenstruum have been treated by the senior author with different hormones without success.

1 ml.) was injected in the skin at the same site (Prausnitz-Kuestner test). Positive skin reactions were also elicited by injection of the serum into normal women during the premenstrual phase (" endogenous passive transfer test ") (Zondek and Bromberg, 1945). Specific densensitization with increasing doses of oestradiol (initial dose 0.001 mg.) given in subcutaneous injections brought relief from this severe disturbance. The patient when last seen, 1 year after treatment, reported a complete cure.

CASE 8. Mrs. S.T. Aged 52. Three years in menopause. Had suffered from severe migraine accompanied by lingual neuralgia since the onset of menopause. Frequent flushes and sensation of peculiar odours and tastes. For a year the patient had been treated with vitamins, hormones and by physiotherapy without success. Hormone cutaneous tests revealed a sensitivity to prolan. Treatment consisted in high doses of testosterone (200 mg.), given with a view to eliminating the allergen (gonadotrophin) through inhibition of the secretion of gonadotrophin by the hypophysis. Following this treatment, the complaints disappeared.

ENDOCRINE ALLERGIC REACTIONS OF THE GENITAL SYSTEM.

Allergy to exogenous allergens should be considered as a possible fact or in the aetiology of such disorders of the genital organs as pruritus vulvae, eczema, leucorrhoea (Rowe, 1928) and dysmenorrhoea (Smith, 1931). Several cases with disorders of the genital function were examined as to hormonal hypersensitivity by the skin test method. Eleven cases of dysmenorrhoea, 5 of amenorrhoea and 7 of menometrorrhagia exhibited negative tests. In premenstrual tension and pruritus vulvae related to menstruation or menopause, on the other hand, positive results were frequent.

(a) *Premenstrual tension*. This group of disorders deserves detailed consideration as it offers a high percentage of positive tests and many cases in which promising results were obtained with desensitization. Premenstrual tension consists of pains in the lower abdomen and back, accompanied often by nervous irritability, depression, severe headache, vomiting and nausea, and less frequently by pains in the breasts and diarrhoea. The symptoms generally begin 1 week prior to, and disappear at the onset of the menstrual flow. The condition should be distinguished from essential dysmenorrhoea which is characterized by cramp-like severe pains in the lower abdomen during the flow. Menstrual dysmenorrhoea is usually conditioned by mechanical, inflammatory, neuralgic or other such factors. The hormone cutaneous tests were negative in a series of such cases (Zondek and Bromberg, 1945).

Out of 33 cases of severe premenstrual tension, 22 showed positive cutaneous reactions to a hormone. In 6 of the positive cases vomiting and nausea accompanied the abdominal pains. Two cases complained of diarrhoea, 2 of pains of the breasts and 12 had pains in the abdomen and back only. The following hormones were found in these cases to act as allergens: oestrone 7 cases, oestradiol 4, progesterone 1, testosterone 5, androsterone 1, and corticosterone 4 cases. Desensitization which was performed in 12 cases gave complete relief in 7, improvement in 2, and no improvement in 3 cases.

CASE 9. Mrs. S.S. Aged 26. Married, never pregnant. Had been suffering for 8 years from premenstrual severe pains in the lower abdomen and from abundant vomiting lasting for 7 days. Six months before, the premenstrual attack had been so severe as to raise the suspicion of acute appendicitis. A subsequent appendicectomy brought no relief. Eosinophilia 9 per cent. Suffered periodically from urticaria. Cutaneous tests revealed a positive response to oestrone. These tests, which were performed shortly after menstruation, evoked a serious general reaction consisting of vomiting, nausea and cramplike pains in the abdomen 24 hours later. By desensitization with allergenic hormone (oestrone) relief from the disturbances

was gained. The patient remained free from symptoms during the following year, at the end of which she became pregnant.

(b) *Pruritus vulvae*. Cases of pruritus were submitted to examination for endocrine allergy after all other investigations had proved negative. In all these cases the complaints or the exacerbation of them related to menstruation or menopause. The duration of illness was at least one year; numerous previous attempts at treatment had been unsuccessful. Positive hormonal tests were observed in 10 out of the 13 cases in which there was an aggravation of the condition during or before menstruation, and in 5 out of the 7 cases related to menopause. The following hormones were found to act as allergens. In the menstruation cases: oestrone 4, oestradiol 1, progesterone 2, testosterone 2, corticosterone 1. In menopause: oestrone 2, testosterone 1, insulin 2. Treatment given in 10 cases was followed in 5 by recovery, in 2 by improvement, and by no results in 3 cases.

CASE 10. Mrs. B.K. Aged 37. Actress. Had been suffering for 2 years from severe pruritus vulvae which seriously interfered with her artistic activities. Menstruation aggravated the condition and led to serious skin changes with eczematous and kraurotic alterations due to secondary infection. Various types of treatment, local and general, had failed to give relief. Blood picture normal. Tests for an endogenous allergen revealed a sensitivity to progesterone, of which 0.01 mg. given intracutaneously sufficed to elicit the reaction. Specific desensitization consisted in subcutaneous injections of minimal but gradually increasing doses of this hormone. The treatment produced a marked improvement, but recurrence of the symptoms followed 2 months later. At this time a second course of desensitization, supplemented by implantation of 25 mg. of progesterone in the form of a pellet and by local inunction of the hormone in the vulvar region was given. The patient has now been free for 1½ years from all complaints and has been able to carry on her career.

CASE 11. Mrs. E.C. Aged 57. In the last 5 years suffered from persistent pruritus vulvae. Attacks had on occasion been so severe as to require morphine. Very poor general condition. Various routine measures (local and general), taken before the patient came to us—had failed to relieve this pruritus. The patient also complained of other allergy manifestations such as asthma and migraine. Blood eosinophilia 8 per cent. Pruritus vulvae and other allergic disorders became aggravated following ingestion of 50 g. of sugar. This observation at first raised suspicion of diabetic pruritus, but a subsequent blood examination showed a normal blood-sugar level of 84 mg. per cent and a glucose tolerance test presented a flat low curve such as is found in cases of exaggerated insulin secretion. It seemed reasonable that the intake of sugar had caused an aggravation of the symptoms because it had evoked increased secretion of insulin and that the latter acted as an allergen. To test this point intracutaneous tests with doses of insulin were carried out. As little as 0.0002 I.U. insulin elicited an urticarial reaction at the site of injection. Injections of 0.1 I.U of insulin with a view to desensitization provoked a severe attack of pruritus vulvae accompanied by strong migraine, general weakness, nausea and anorexia. The desensitization was performed with minimal doses of insulin, given subcutaneously and by local inunction. In this way relief from all the symptoms was obtained for 6 months. A relapse was treated with local inunctions of insulin ointments (2 units of insulin pro 1.0 g. of lanolin vehicle). Complete freedom from symptoms was maintained by the repetition of desensitization treatment every half year.

ENDOCRINE ALLERGIC REACTIONS OF THE OCULAR SYSTEM.

We have found that certain cases of ocular diseases of unknown origin may depend upon endocrine allergy. The cutaneous tests with hormones showed a positive response in 1 case of chronic recurrent conjunctivitis, and in 3 cases of superficial keratitis.[8] The ocular manifesta-

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Superficial Keratitis. Out of 3 cases of superficial keratitis of unknown origin,[9] 2 were found sensitive to corticosterone and 1 to androsterone. The beneficial influence of desensitization in the 2 corticosterone sensitive cases was quite remarkable.

CASE 12. Mrs. R.F. Aged 41. Suffered during the last 4 years from superficial keratitis which became aggravated regularly during the last week of the menstrual cycle. At such times the corneal changes were pronounced, ocular vision was very limited, and severe ocular discomfort associated with excessive tear-shedding appeared. The symptoms had obliged the patient to suspend normal activity for about a week each month. Various ophthalmological treatments brought no relief. Urticaria had been experienced some years before. Blood eosinophilia 5 per cent. No allergy had been recorded in the family history. The endocrine allergy tests revealed sensitivity to corticosterone. Desensitizing treatment with this hormone produced most impressive results: the subjective complaints subsided completely; the corneal opacities were found at ophthalmological examination to have disappeared. During a period of observation which lasted 2 years, no recurrence of discomfort in vision occurred, and at the end of this period the patient was released as cured.

ENDOCRINE ALLERGY AS A CAUSE OF PREMENSTRUAL FEVER.

Fever appears rarely in allergy. It can be elicited by certain exogenous allergens (serum sickness, drug allergy, certain cases of hay-fever, etc.), and may occasionally be observed during the premenstrual period. In several cases observed by us high premenstrual temperatures were followed by normal temperature throughout the first phase of the menstrual cycle. These time relations strongly suggest the existence of some connection between the manifestations of fever and the secretion of the sexual glands.

Premenstrual fever. Three women in whom fever with temperature as high as 39°C. recurred in the last week preceding menstruation were positive in cutaneous hormone tests, 1 to oestrone and 2 to testosterone. Desensitization by administration of increasing doses of the allergenic hormone was performed in 2 of these cases (1 oestronè and 1 testosterone). In both cases the treatment procured absolute relief.

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(a) Specific desensitization and its mechanism.

The ultimate aim of the specific desensitization is the protection of the diseased organ (shock organ) from the reaction between its cellular fixed antibodies and the allergen. It is achieved by the regular administration of small, increasing amounts of the allergen into the skin tissue. Under this treatment free antibodies are formed, circulating in the blood; when the offending antigen enters the blood stream, it is bound by free antibodies and cannot react with the fixed ones of the shock organ. Unfortunately the free antibodies are rapidly eliminated after the discontinuance of the treatment, and the renewed contact with the allergen may then induce allergic reactions. Therefore, in treatment of allergic diseases, it seems advisable to maintain the supply of small amounts of allergen for a long period of time. In endocrine allergy, the slow and prolonged desensitizing action of hormonal allergen is obtained by subcutaneous injections of oily solutions of steroid hormones, since these substances, not being easily soluble, require a relatively long period of time for their absorption; furthermore, the " depôt method " by implantation of small crystalline pellets of steroid hormones (described below) provides a slow and continuous supply of minimal amounts of the allergenic hormone. However, the antibodies in circulating blood formed by minimal amounts of the allergen are not always sufficient to protect the shock organ, since any massive re-exposure to the injurious substance may elicit allergic reaction, even during the course of desensitization treatment.

The skin, through its selective function in immunity reactions, seems also to intervene in the mechanism of desensitization (Heise, 1945). In fact, proofs are available that the skin is particularly active in anti-body production (Tufts, 1937), and may bind by its cellular antibodies considerable amounts of the allergen. It seems also possible that during the course of desensitization, the skin injected with the allergen may act as an additional shock organ and neutralize at the skin site those quantities of the allergen which have not been bound by the free blood antibodies (Heise, 1945). The skin seems also to participate in the desensitization mechanism of endocrine allergen. The frequent reactivation of the previous intracutaneous tests when the hormonal allergen reaches its peak concentration in the body (either after injection, " recurrent reaction ", or spontaneously, " retarded reaction " and " periodic retarded reaction ") points to the antigen-antibody reaction at the skin site. The skin acting as an artificially produced shock organ may occasionally protect the original allergic tissue, and thus prevent the allergic manifestation.

The following methods have been used for specific desensitization of endocrine allergic manifestations :

1. *Subcutaneous injections.* In this method, antigenic hormone is injected in small but gradually increasing amounts, at regular intervals, usually one day. Three concentrations of steroid hormone in oil (0.01 mg./ml., 0.1 mg./ml., and 1 mg./ml.) are prepared. Before beginning the treatment the sensitivity of the patient is estimated on the basis of a check test in which 0.1 ml. amounts of the mentioned solutions (equivalent to 0.001, 0.01 and 0.1 mg. amounts of the allergenic hormone) are given intradermally. Treatment is usually started with a subcutaneous injection of the smallest dose in oil which elicited a positive intracutaneous reaction in the check test. If a general reaction (urticaria, headache, vomiting, fever, etc.) is evoked by the cutaneous test, an even smaller dose of the specific allergen had best be

used to start with. The injections are given once daily, the dosage of allergen being stepped up gradually to a maximal single dose of 1 mg. The total course of treatment generally comprises 20 to 30 injections. The rate at which the allergenic hormone dose can be increased depends on the reactions of the patient. These may be of 2 kinds: local and general. The local reactions are characterized by the appearance of reddening and itching at the site of a previous intradermal test ("recurrent reaction"), or by pains and infiltration at the site of a desensitizing injection. Increase of dose should not be attempted before disappearance of these reactions. The general reaction is characterized by fever, urticaria, headache, vomiting and nausea. Any of these symptoms is a contra-indication of dose increase.

In desensitization to insulin, the hormone in aqueous solution (1 ml. = 1 I.U.) was injected in doses which were gradually increased from 0.1 to 1.0 units. In desensitization to chorionic gonadotrophin, korotrin in aqueous solution was injected in doses which were increased from 1 to 100 units. Our limited experience of sensitivity to gonadotrophin does not permit definite conclusions as to the efficacy of this method of desensitization.

2. *Implantation of hormone-pellets* ("*depôt method*"). In some patients, relapses occurred a few months after the injection treatment, and thus showed that the desensitization induced had only been temporary. A second course comprising 10 injections, starting from a dose of 0.1 mg., which was gradually increased to 1.0 mg., was instituted in these cases, and at its completion a pellet containing 15 to 25 mg. of the antigenic steroid hormone was implanted. It might be feared that the deposition of a pellet containing a significant dose of antigenic hormone could possibly

reactivate the allergic reaction. However, this mode of treatment proved efficacious and elicited no harmful side-reaction.

Other authors (Geber, 1939: Urbach, 1943) have employed another "depôt method" in desensitization treatment by repeated intracutaneous injections of the allergen at the same skin site, also with good results.

3. *Percutaneous desensitization*. It has been shown by us that genital hormones can be absorbed by the body through the skin (Zondek, 1929: 1935b). We have made use of this property to effect specific desensitization. Apart from the local effect so induced in the affected tissues, desensitization is obtained because of the penetration of hormone into the circulation. This percutaneous method was employed, alone and in combination with injections, in 4 cases of pruritus vulvae and in 4 cases of acne. 1 to 2 mg. steroid hormone in lanolin (1 mg. of hormone in 1 g. of vehicle) was applied percutaneously daily.

The local method of desensitization by application of gradually increasing doses of allergen ointment on the affected tissue has a widespread use also in other forms of allergy, especially in various forms of allergic dermatitis (Mackenzie and Baldwin, 1921: Gongerot and Meslin, 1938). However, this method does not permit accurate dosage of the allergic hormone applied, and the desensitization requires a long-lasting period of treatment.

Results of specific desensitization.

Desensitization treatment in its various modifications has now been applied in a total of 47 cases (Table II). In this group, 24 patients (51 per cent) recovered, 13 (28 per cent) improved, and 10 (21 per cent) showed no amelioration. Untoward effects from the treatment were rare and consisted in fever (38°C.) 2 cases, nausea and vomiting 2 cases, headache 1 case, and urticaria 1 case.

(b) Elimination of Allergenic Hormone by specific interference with its Production.

The observation that large doses of oestrogen or testosterone may inhibit the gonadotrophic function of the hypophysis (Zondek, 1936a; 1936b; 1937; 1938; 1940; 1941a : Geist, 1941 : Salmon, 1941) made it possible to eliminate certain hormones from the circulation. We employed this method in 2 cases in order to spare the organism contact with the allergenic hormone. In one case sensitive to gonadotrophic hor-had undergone an operation for cancer of the breast 3 years earlier). Administration of testosterone in high doses (400 mg.) was followed by recovery. This method of treatment, namely, administration of large doses of oestrogens or androgens to cause pituitary inhibition, is not advised for regularly menstruating women, since the inhibition of the gonadotrophic function so induced delays menstruation (Zondek, 1936c : 1941b). The method should be applied mainly on menopause patients who show sensitivity to gonadotrophic hormone,

TABLE II.

Results of Desensitizing Treatment.

Diseases treated	Number of cases treated	Desensitization treatment	Treatment through inhibition of pituitary secretion	Recovery	Improvement	No results
Asthma	3	3	—	1	2	—
Vasomotor-rhinitis	2	2	—	1	1	—
Angioneurotic oedema	2	2	—	2	—	—
Chronic urticaria	4	4	—	2	2	—
Chronic eczema	1	1	—	—	—	1
Acne	3	3	—	—	2	1
Migraine	8	7	1	4	2	2
Superficial keratitis	2	2	—	2	—	—
Premenstrual tension	12	12	—	7	2	3
Pruritis vulvae	10	9	1	5	2	3
Premenstrual fever	2	2	—	2	—	—

mone with migraine in menopause, the production of the allergenic hormone was inhibited by the administration of high doses of testosterone (400 mg. of testosterone propionate in 8 days). Recovery was effected by this treatment (case 8). In a case sensitive to oestrone with pruritus vulvae in early menopause, the administration of oestrone was contra-indicated in view of the carcinogenic disposition (patient oestrone, or to testosterone. In cases of sensitivity to gonadotrophic hormone, the hormonal allergen may be eliminated by administration of high doses of testosterone or oestrogens. If testosterone is the allergen, inhibition of its production will be produced by high doses of oestrogenic hormone. In cases of sensitivity to oestrogens, on the other hand, testosterone should be employed for pituitary inhibition.

COMMENT.

Allergic manifestations are elicited as a rule by exogenous antigens. The observations reported in this paper demonstrate the possible existence in man of allergic sensitivity to endogenous secretory products of the endocrine glands. This peculiar condition is readily comprehensible in relation to the protein or protein-like secretions, e.g., anterior and posterior pituitary hormones, thyroid hormone, insulin, and chorionic gonadotrophin. It has been assumed (Glass, 1936) that premenstrual headache can be due to hypersensitivity to the pituitary gonadotrophic secretion. Furthermore Lowell (1942) found that positive cutaneous reactions are induced by an intracutaneous injection of an extract of human pancreas. Urbach (1939) explained the aggravation of acne and eczema during the pre-menstrual phase as due to the presence in the blood of such patients of an endogenous allergen. His patients showed positive skin reactions to their own serum. The existence of allergic reactions to steroid hormones is a less expected observation. Allergic reactivity to steroid hormones can be demonstrated by intradermal injection of the steroid allergen in a vehicle of oil. It is known that various oils can evoke reactions of an allergic nature. However, olive oil prepared according to the prescription of the Pharmacopeia Helvetica and heated for at least 48 hours at 100°C. produces such reactions in only 7.5 per cent of healthy cases. No ideal uniformity in different vehicles has yet been found. Individuals sensitive to oil alone were therefore excluded from the case material of this study. In a certain number of patients with positive cutaneous reactions to oestrone or oestradiol in an oil vehicle, positive reactions were also obtained when the hormones were given in physiological saline when they were injected intradermally.

Cases sensitive to testosterone in oil reacted allergically to this hormone also when it was injected intradermally in the form of a suspension of crystalline testosterone in normal saline. These observations constitute a further proof that the allergen of the reported cutaneous reactions is in fact the steroid hormone rather than its vehicle.

As has been shown, blood from a patient hypersensitive to a steroid hormone contains a specific reagin to the hormonal allergen (Zondek and Bromberg, 1945). Serum of such a patient when it is transferred into the skin of normal women elicits a positive Prausnitz-Kuestner reaction. In certain cases, serum containing such a reagin elicits the positive skin reaction when the concentration of allergenic hormone in the body of the normal subject climbs to a sufficient level (" endogenous passive transfer test "), e.g., at physiological peak, or after injections of the allergenic hormone.

Allergic manifestations (like asthma, hay-fever, urticaria, etc.) can be caused not only by exogenous glands but also by endogenous secretory products of the endocrine glands acting as allergens. In general, however, the latter aetiology should be taken as a probable explanation only where the clinical manifestations are related to the genital functions.

It has been found that premenstrual pain and various other premenstrual disorders (nausea, vomiting, fever, etc.) are often of an allergic nature. The same symptoms have a different origin when they occur during menstruation. Pre- and intramenstrual disorders seem, in other words, to be aetiologically entirely different. Allergic dysmenorrhoea characterized by pain before the menstrual flow must thus sharply be separated from essential dysmenorrhoea in which pains occur during menstruation. Essential dysmenorrhoea cannot be regarded as an endocrine allergy

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condition, since in 11 cases of this kind examined by us, cutaneous tests revealed not a single positive response.

A varied range of clinical manifestations related to menstruation or menopause (pre-menstrual tension, migraine, urticaria, and pruritus vulvae) may be due to endocrine allergy, though they need not necessarily be of this origin. On the other hand, hyper-sensitivity to different hormones can become manifested clinically in the same disorder. Thus, out of 5 cases of chronic urticaria, 2 were found to be associated with sensitivity to oestrone, while the remaining 3 cases were associated respectively with sensitivity to progesterone, testosterone and cortico-sterone.

In the treatment of pruritus vulvae by percutaneous inunction of steroid hormone as introduced by the senior author (B.Z.), it is probable that desensitization of the patient by means of small amounts of resorbed hormone (about 15 per cent) is the factor responsible for the favourable results which are obtained. The fact that a given percutaneous ointment treatment relieves pruritus vulvae in some cases and not in others is readily comprehensible under this view which postulates the existence of a *specific* hormonal allergen. The method of intracutaneous tests makes it possible to determine with greater pre-cision the hormone which it is proper to apply in this way.

Our study of endocrine allergy has been made exclusively in women, as in them the cyclic nature of the genital functions pro-vides a convenient means of demonstration of the existence of an endocrine allergic condition. The available evidence points, however, also to the existence of conditions of hypersensitivity to endogenous hormones in human males as well. It seems not unlikely that the intracutaneous test technique will prove useful as a means of detecting conditions of this kind in men.

In *normal* women with regular periods the cutaneous reaction to the hormones tested was in no case found to be positive. The high level of the incidence of endocrine allergy in the cases reported above results from case selection and should not be regarded as forming evidence that endo-crine allergy is a frequent occurrence. The cases we have described were all selected from a group which had proved resistant to all common methods of treatment, and in which the symptoms of the complaint related to the genital functions. In general practice, endocrine allergy is not often encountered.

SUMMARY AND CONCLUSIONS.

1. Sixty-six cases in which sensitivity towards endogenous hormones gave rise to various pathological manifestations are reported. Hormonal allergy was detected by skin tests with oily hormone solutions injected into a layer of the epidermis deeper than that used for ordinary skin tests with aqueous solutions.

2. In healthy women endocrine allergic conditions of this nature were never en-countered at any phase of the sexual cycle.

3. Endocrine allergic conditions are not frequent. They have a considerable rate of incidence, however, in disturbances related to menstruation or menopause.

4. Clinical manifestations of " endocrine allergy " as so far encountered have been divided according to the organs thus in-volved. The possible clinical involvement in such cases of the respiratory, cutaneous, nervous, genital and ocular systems is illustrated.

5. The following ailments have been identified as due in certain cases to " endo-crine allergy ":

(a) Respiratory tract: asthma and vasomotor rhinitis;

(b) Cutaneous system: angioneurotic oedema, chronic urticaria and acne;

(c) Nervous system: migraine;

(d) Genital system: premenstrual tension and pruritus vulvae;

(e) Digestive system: nausea, vomiting, diarrhoea and epigastric pains during the premenstrual phase;

(f) Ocular system: chronic, recurrent conjunctivitis and certain forms of keratitis (as superficial keratitis and keratitis rosacea);

6. The following 4 methods of treatment for endocrine allergy are proposed:

(a) Desensitization by the subcutaneous injection of the hormonal allergen in question in a series of doses of gradually increasing size;

(b) Desensitization by the "depôt method" involving the implantation of hormone-pellets. This method is applied after it has been advanced to a point at which the patient can already tolerate a fairly high dose of the hormone in question;

(c) Desensitization by percutaneous treatment with hormone ointment;

(d) Elimination of the allergenic hormone from the body by the inhibition of the gonadotrophic hypophyseal function with large doses of oestrogens or androgens.

7. In 47 cases of endocrine allergy treated by specific desensitization the following results were obtained: complete recovery in 51 per cent, improvement in 28 per cent, and negative results in 21 per cent. In 2 cases the allergenic hormone was eliminated by the inhibitory effect of high doses of tostesterone on pituitary secretion.

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The Use of Radiology in Predicting Difficult Labour *

BY

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Lecture 2: Forecasting the Course of Labour

Features of a Good Obstetric Pelvis

Among the various anatomical features revealed by radiography the following are tokens of easy delivery:

The obstetric conjugate is adequate in size. This diameter is measured on the lateral radiograph from the inner margin of upper part of the pubic bone to the nearest part of the sacrum—which may be the promontory itself or, more usually, a point below the promontory at which the brim outline is seen to intersect the sacrum.[25] This and other measurements are shown in Table I. Two hundred years ago, Smellie stated that the *true* conjugate (which is about 5 mm. greater than the *obstetric* conjugate) measured $4\frac{1}{4}$ inches (10.8 cm.), and this low value seems to have been widely quoted in subsequent obstetric literature. Greulich and Thoms[15] and Nicholson[16] have brought forward good reasons for supposing that the size of the brim conjugate is largely dependent on diet during adolescence, and in a recent investigation of healthy women in a rural community a

value as high as 12 cm. ($4\frac{3}{4}$ inches) has been obtained for the obstetric conjugate (Nicholson).

The sacrum shows a full, even curve from above downwards. In consequence, the sacro-sciatic notch should be wide, and almost as open below as it is above (Fig. 7, D). The wide sweep of the sacrum also gives an adequate lower antero-posterior dimension to the pelvis, measured from the inner lower border of the symphysis to the tip of the sacrum (Table I). Sometimes the first coccygeal segment is fused to the sacrum; and if the coccyx also projects sharply forward (Plate XI, B and C) it may then obstruct delivery. Allowance should be made for this possible abnormality when measuring the lower antero-posterior diameter. I conveniently call this modified measurement the *available* lower antero-posterior diameter (see also later section). Occasionally, an inward-pointing coccyx may be dislocated or even fractured during the birth of the head—an event sometimes encountered when traction is made on the forceps to overcome an arrest of the head in a low pelvic position (Plate XI, D).

The pubic bone and its descending ischial rami are nearly parallel to a line joining the sacral promontory to the sacral tip. Any marked convergence from above downwards indicates the possibility of outlet con-
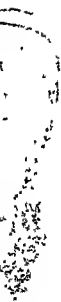

PLATE XI.

Variations of the coccyx. A Normal coccyx being pushed back by the descending foetal head B. Inturned coccyx with fused sacro-coccygeal and inter-coccygeal joints C. Coccyx sharply inturned. D. Coccyx fractured (or dislocated) at inter-coccygeal joint following arrest of head at outlet (low forceps delivery).
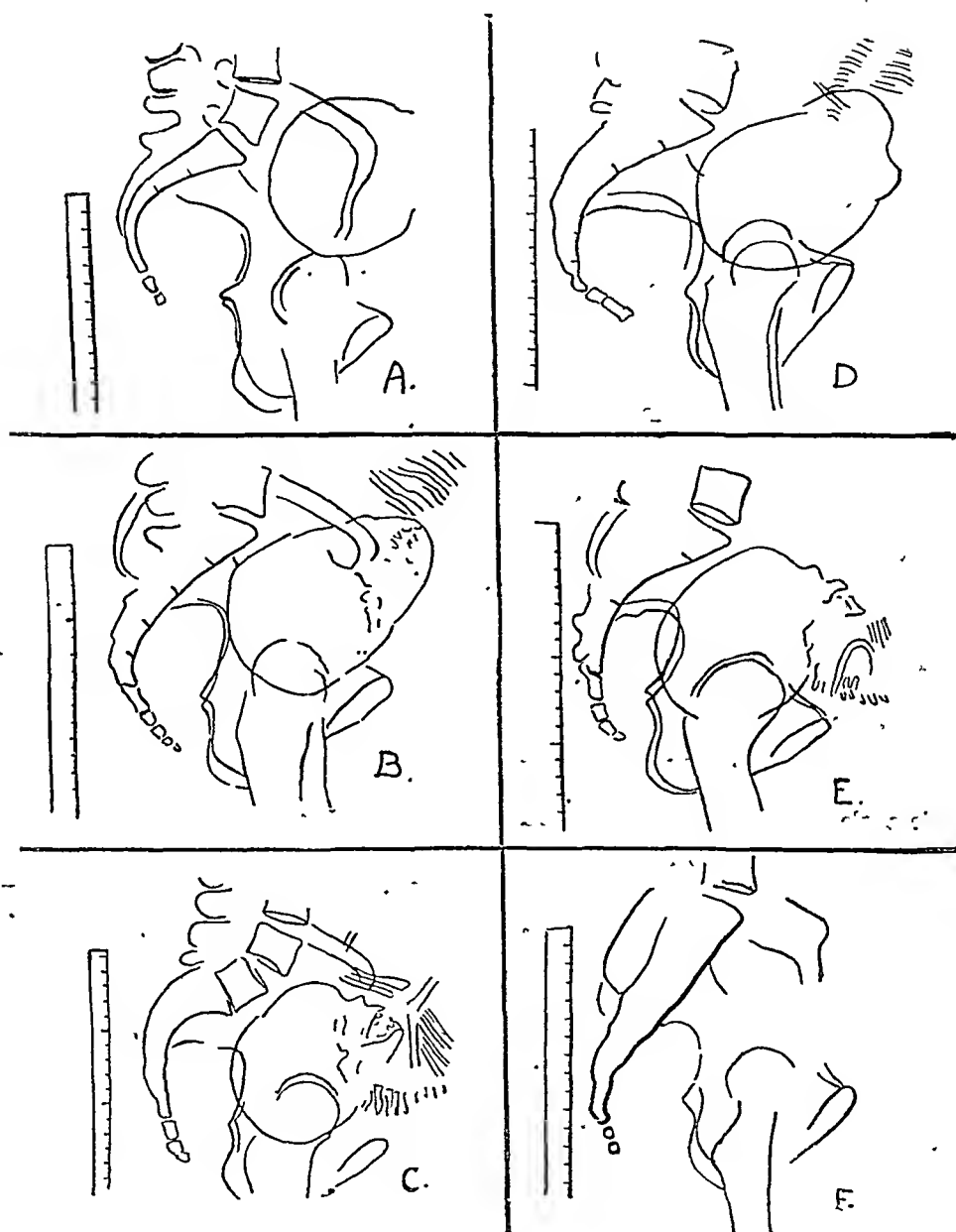
C. M.

FIG. 7.

Tracings obtained from lateral radiographs. A. Short sacrum (shallow pelvis). B. Long sacrum (deep pelvis). C. False promontory. D. Wide sacro-sciatic notch. E. " Closed " sacro-sciatic notch. F. Flat sacrum.

traction (Fig. 7, E). A more accurate indication of this latter feature is the size of the posterior sagittal diameter of the outlet; a point is marked midway between the ischial tuberosities (if these are not already android* pelvis of Caldwell and Moloy) is unfavourable because the widest transverse diameter is too near the sacrum to be available for the foetal head (Plate III). This feature can also be described by say-

TABLE I.
RADIOGRAPHIC MEASUREMENTS OF THE PELVIS
(Average values, with Standard Deviations in brackets.)

	Nicholson	Ince and Young	Oxford. Selected, but spontaneous delivery	Oxford. Unselected
Obstetric conjugate ...	11.6 (1.0)	11.8 (1.0)	11.2 (0.9)	11.8
Transverse of brim ...	13.2 (0.76)	13.1 (0.7)	12.6 (0.6)	12.9
Available transverse brim	—.	—.	—	12.4
Lower antero-posterior ...	13.0 (0.96)	12.0 (0.86)	—	—
Available lower antero-posterior ...	—	—	11.4 (0.9)	11.7
Bi-spinous	10.5 (0.77)	9.95 (0.71)	10.1 (0.7)	10.45
Posterior sagittal of outlet	—	—	8.6 (0.9)	8.9
Sub-pubic angle	84.8° (7.3°)	—	81.2° (7.3°)	86°

superimposed) and the distance measured from this point to the tip of the sacrum, or to the first inter-coccygeal joint if the coccyx is fused to the sacrum (Table I).

The transverse diameter of the brim is adequate, and the posterior segment of the brim outline is well rounded. The dimension of the transverse diameter is shown in Table I. Usually it exceeds the obstetric conjugate by about 1.5 cm. If the two are equal, or if the antero-posterior exceeds the transverse (dolichopelly, or "anthropoid" pelvis (Plate II), an occipito-posterior position of the head will usually result. This was first pointel out by Thoms[17] in 1932 and has been amply confirmed by subsequent workers. A wedge-shaped brim (the

ing that there is a short posterior-sagittal diameter of the brim.

* Investigations by Thoms and Greulich (*Amer. Journ. Obstet. and Gynecol*, 1940, xxxix, 56), and by Ince and Young (*Journ. Anatomy*, 1940, lxxiv, 374), have shown that the brim of the male pelvis is usually well rounded and has no special tendency towards a wedge shape; it is therefore singularly inappropriate that this type of brim should be termed "android". But the male pelvis has a narrow pubic arch and a smaller bi-spinous diameter than has the female pelvis, and there is also a distinct tendency to funnelling from above downwards—features which if found in a female pelvis do merit the term "android". There is no close relationship between the shape of the brim and the shape of the outlet.

If the shortened posterior sagittal diameter is continued into the pelvic cavity, as evidenced by a flattened sacral curve, prognosis is considerably worsened.

The limbs of the pubic arch diverge widely enough to accommodate the head with little wastage of space under the apex of the arch. A narrow arch will cause the head to be forced backwards with consequent danger of severe (third degree)

studied in the lateral X-ray of the pelvis. The average bi-parietal diameter is about 9.3 cm. A diameter of more than 9.6 cm. represents a distinctly large head with corresponding likelihood of difficulty during delivery. The relationship of the head to the pelvis is of special importance. Usually the long diameter of the head lies in, or nearly in, the transverse diameter of the brim; and normally there is space

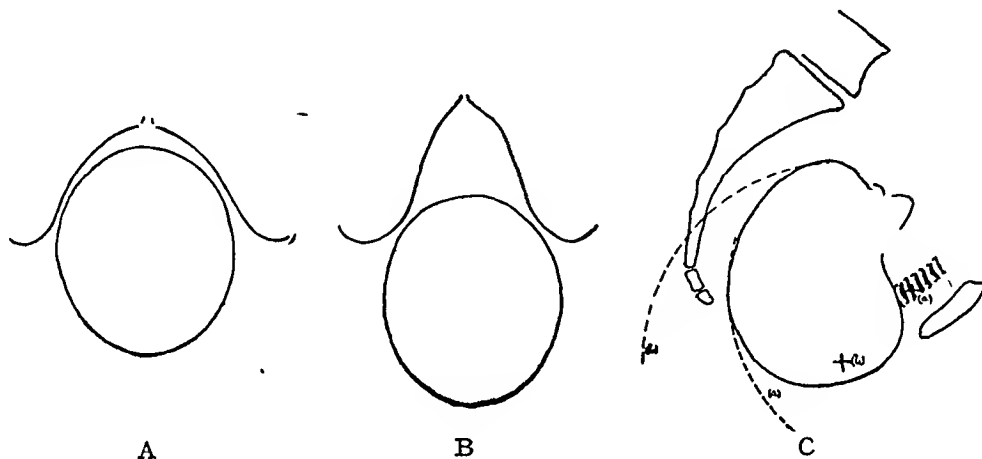A   B   C

FIG. 8.

A narrow pubic arch pushes the foetal head further back with risk of severe perineal tear. If there is also a forward-projecting sacral tip, obstruction may result. The arches shown in A and B are actual tracings obtained from radiographs. (Redrawn from Nicholson, *loc. cit.*)

perineal rupture (Fig 8). If the narrow arch is also associated with a forward projecting sacral tip or fused coccyx (causing a shortening of the lower antero-posterior, and posterior sagittal outlet diameters) delivery may be arrested by an outlet obstruction. It is in this latter type of case that a well-timed symphysiotomy is sometimes a conspicuously successful operation. The average measurements of the subpubic angle and of the posterior sagittal are shown in Table I.

The foetal head is moderate in size relative to the pelvis and is favourable in position. The size, relationship to the pelvis, position and level of the foetal head are all best

to spare between the parietal bones and the pelvic walls, both in front and behind (Fig. 7). The head should be well flexed; usually it is also tilted towards its posterior shoulder. The position of the head is best ascertained by identifying the relative positions of the foetal vertebral column and the mandible.

THE INTERPRETATION OF
RADIOGRAPHIC FINDINGS.

The various radiographic features just mentioned are used to " size-up " a case of supposed cephalo-pelvic disproportion, but their interpretation, even for an experienced worker, necessarily calls for much care and

judgment. Many attempts have been made to simplify matters.

Area Measurement. Nicholson[18] has stressed the importance of the *brim area* which, he has shown, can be approximately estimated by assuming that the brim is elliptical, and using the appropriate formula (π. times half the minor, multiplied by half the major axis). He states that when the area is reduced to 90 sq. cm. the level of uncertainty is reached; or, more exactly, that a brim with an area of 110 sq. cm. can pass 99.9 per cent of heads; a brim of 100 sq. cm. can pass 97 per cent; a brim of 90 sq. cm. can pass 70 per cent; but that a brim of 80 sq. cm. can pass no more than 21 per cent of foetal heads.[19] While not routinely measuring the foetal head, he estimates that for easy delivery the relationship of the area of the head at its bi-parietal level—which he assumes is circular—to the area of the brim should not exceed 70–80 per cent.[20]

Nicholson maintains that although pelvic brims vary considerably in shape (pelvic index), those with equal area have equal obstetric value. In making a prognosis he lays emphasis on the pelvic rather than on the foetal size.

The area required at the level of the ischial spines—"the plane of least pelvic dimensions"—is less than that required at the brim. According to Nicholson an uncertainty is caused by the fact that in many cases the lower part of the pelvis expands during the labour so that an easy delivery may take place even when difficulty seemed inevitable. (I am fully in accord with this opinion, and believe that the bi-spinous diameter in particular increases under the influence of the outward thrust exerted by the descending foetal head.)

Unquestionably, Nicholson's method of area measurement is helpful, although there are many cases (e.g. those in which the foetus is unusually big or unusually small) in which it must leave the obstetrician in some doubt regarding the outcome of labour.

Pelvic Charts. Early in his work Thoms[21] devised a "pelviscope" by which a tracing could be made from the radiograph showing the true size and shape of the pelvic brim. Some years ago I[22] proposed adding the outline of the flexed head to the tracing so obtained, thus making it possible to reveal in a more obvious form the main features of the cephalo-pelvic relationship that is likely to obtain when the patient goes into labour (Plate XII).

Rohan Williams[23] has recently used a somewhat similar method which he has developed further by adding a chart of the lateral view of the pelvis (reduced to true size). On these charts he superimposes a circle representing the size of the foetal head. By thus picturing the pelvis in two projections he finds that he can forecast the course of subsequent labour with a considerable degree of accuracy. In a very recent publication[24] he presents excellent results by the use of this method.

Despite these favourable remarks, this approach to the problem is not, in my opinion, completely satisfactory. Firstly, the construction of the charts is an exacting and time-consuming occupation. Secondly, the fault hitherto so manifest in this class of work—namely, that radiographic interpretation is impressionistic rather than factual—is not entirely overcome.

The Graph Method. This brings me to the focal point of these lectures, and I now wish to present a method which has gradually evolved in the course of my investigations and which has greatly simplified the interpretation of the radiographs.

As the head descends through the pelvis from brim to outlet it passes through a

channel constantly varying in shape. Ideally, therefore, one should record the shape and size of an infinite number of cross sections of the birth canal, and ascertain for each the cephalo-pelvic relationship. This is impracticable; but for general purposes it is sufficient to consider the antero-posterior and the transverse diameters of (1) the brim, (2) the pelvic cavity at the level of the ischial spines, and (3) the outlet. It is now necessary to define these levels more exactly, particularly as none of them, strictly speaking, is a true plane.

The Brim. Contrary to orthodox teaching the promontory of the sacrum is not usually the important posterior landmark; this is because the outline of the brim—as can be seen by examination of a dried pelvis—crosses the sacrum and naturally terminates at the junction of the first and second sacral segments, or at a point between that and the promontory.[25] This dimension is often a few millimetres less than the conventional obstetric conjugate. In this work the *Antero-posterior Diameter* of the brim means the shortest distance between the upper and inner margin of the symphysis pubis and the nearest part of the sacrum—usually the point just mentioned, but sometimes, if the sacrum is short or is well curved, the promontory itself.

Again contrary to orthodox teaching, the greatest transverse diameter of the brim is not the measurement that is found to be of chief value. In my work the transverse measurement refers to a diameter which intersects the conjugate of the brim at the mid point; this measurement I conveniently designate the *Available Transverse Diameter*. The reason for this selection is as follows: In a round (gynaecoid) pelvis the widest transverse dimension is situated well forward, coinciding, or nearly coinciding, with the available transverse diameter: in a pelvis of this shape the foetal head can make full use of the space available at the brim, and prognosis is, generally speaking, good. If, however, one is dealing with a pelvis showing a wedge-shaped brim, the widest transverse diameter is situated near to the sacrum: the foetal head cannot then make use of the space available and the prognosis is correspondingly bad. In this latter case the available transverse diameter

is far in front of the widest transverse diameter and measures much less; it therefore furnishes a better indication of the restricted obstetric value of this type of pelvis.

The Cavity. The lower antero-posterior measurement is taken from the nearest point of the inner margin of the symphysis pubis to the tip of the sacrum. If the coccyx is seen to be fused with the sacrum the measurement is taken to the first free intercoccygeal joint. Sometimes it is impossible to be sure of the mobility of the sacro-coccygeal joint from X-ray examination, and it is then necessary to make a clinical test; a finger is passed into the rectum, the coccyx is gripped between the forefinger and thumb, and the point where movement takes place is identified.

The *Transverse Diameter of* the cavity is reckoned as the distance between the ischial spines.

The Outlet. Various methods of estimating the obstetric value of the outlet have been tried. The simplest is to measure the sub-pubic angle and, as will be explained, to use this measurement in conjunction with the posterior sagittal dimension of the outlet. (These measurements have been defined in a previous section.)

The evolution of the present method can now be explained. Three types of charts were prepared, one for the brim, one for the cavity and one for the outlet. In each, the antero-posterior dimensions were marked vertically, and the transverse dimensions horizontally. By pin-pointing a spot on each of the three charts the main facts regarding the size and shape of any particular pelvis could be recorded.

Separate sets of three charts were made for each size of foetal head from 9.0 cm. to 9.9 cm. bi-parietal diameter—that is, 10 sets of charts in all. (Cases in which the head measured less than 9.0 cm. were discarded from the present investigation.)

All the collected cases for which complete radiological and clinical data were available (including the post-natal measurement of the bi-parietal diameter of the head made by myself) were now entered on the charts. For each easy delivery a cross was made and for each difficult delivery a nought.

The definitions adopted for easy and difficult delivery were as follows. By *easy delivery* was meant a spontaneous delivery occurring within 30 hours in a primigrávida, or 24 hours in a multipara. (If uterine contractions definitely ceased for a long period during the labour this fact was taken into consideration, but an adjustment of this nature was made in very few cases.) By *difficult delivery* was meant a labour in excess of the above-stated times (with the same reservation), or a delivery

almost all the "difficult" deliveries fell on to the lower and left side of one or other —or a combination—of the three charts. A dividing line could be marked out on each chart which substantially separated the one class of case from the other. Thus each chart sifted out, as it were, the type of case in which difficulty at that particular level was encountered (Fig. 9).
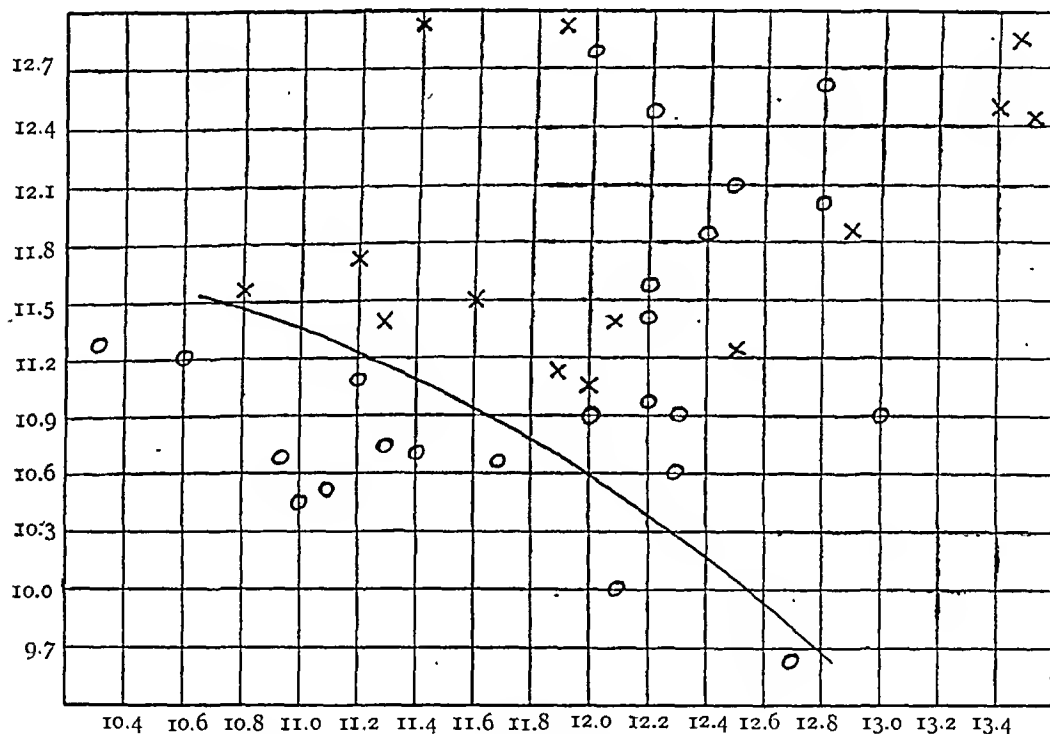

FIG. 9.

Specimen chart showing easy and difficult deliveries arranged in accordance with brim size (see text). Antero-posterior brim measurements are recorded vertically, and available transverse measurements are recorded transversely. This chart deals only with foetal heads of 9.5 cm. biparietal diameter. Note that a line can be drawn on one side of which no easy deliveries take place. Most of the difficult deliveries recorded on the "easy" side of the above chart were "sieved out" by the companion cavity and outlet charts.

requiring forceps, or a delivery requiring Caesarean section after a trial of labour.

When the completed charts were examined it was at once apparent that the majority of "easy" deliveries fell on to the top right-hand part of each chart while

Having marked out the dividing line on each individual chart, it was then possible to combine the charts and to draw up a single set of three charts showing the dividing lines for easy and difficult deliveries for each size of foetal head (Fig. 10).

These are now the key charts on which it becomes a quick and easy matter to pin-point any pelvis and to define its obstetric value relative to the estimated size of the foetal head. It should be noted that the

FIG. 10.

Charts showing levels at which difficulty (as defined in text) may be anticipated for each size of foetal head.

dividing lines have been drawn up on a pure "trial and error" basis, they are not compiled on any mathematical formula.

Results. The cases on which this investigation was based were far from unselected. There was heavy loading with (1) patients showing a high head at term or other clinical evidence of disproportion, and (2) puerperal patients who had had an unexpectedly difficult time in labour and who were therefore examined retrospectively. This high rate of selection has proved both an advantage and a disadvantage. On the one hand it enabled a large number of cases to be investigated of the type most useful in constructing the required graphs. On the other hand there was the disadvantage that the high proportion of border-line cases made the same material unsuitable as a fair test of the value of the graphs in indicating the probable course of labour in the general run of cases. (Even if some perfect form of pelvimetry and cephalometry could be evolved in which every possible error had been eliminated, the forecast, if restricted to a simple "yes" or "no", could not achieve more than a 50 per cent accuracy when applied to a *strictly* border-line group.)

A further difficulty arose from the fact that the second group just mentioned inevitably included many cases in which dystocia was caused by uterine inertia or other abnormality quite distinct from cephalo-pelvic disproportion. In other words, no one can say that in a particular case labour *cannot* be difficult or prolonged. Unexpected happenings of this sort are not therefore a disparagement of the value of the proposed method of assessing cephalo-pelvic relationship. For what they are worth the figures in this group are these: a favourable outcome was indicated in 89 cases; of these, an easy delivery did, in fact, occur in 64.

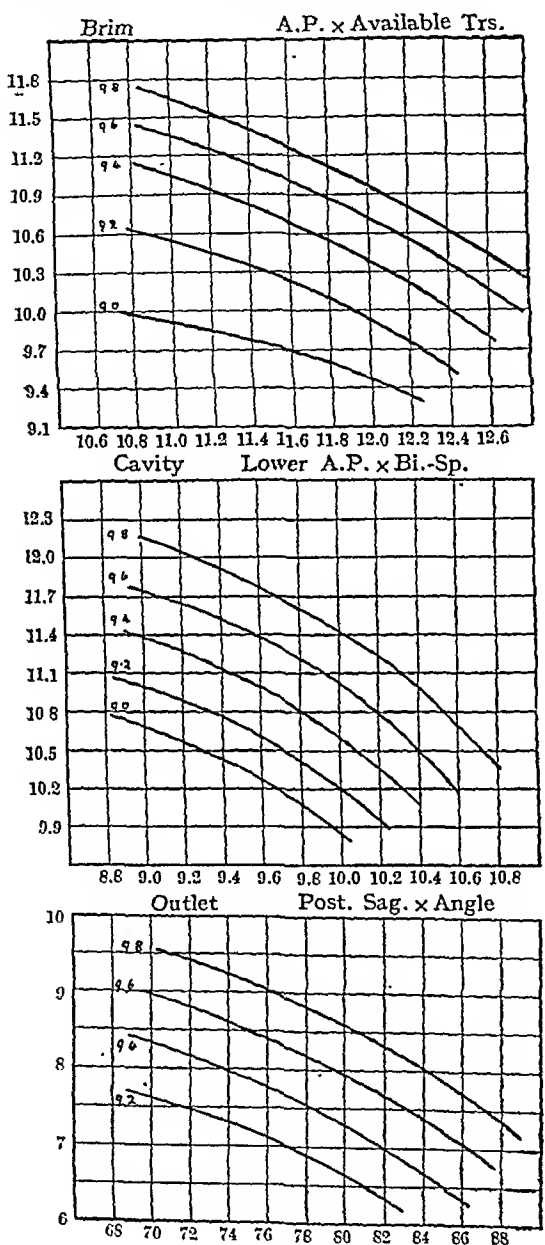Much more interesting and useful is the

group of cases in which *difficulty* was indicated. In it a considerably higher accuracy of prognosis was found. Whereas in the previous group (the "favourable-forecast" group) certain influences sometimes made their appearance and caused the prediction to be upset, these influences if they appeared in the second group (the "dystocia-forecast" group) now operated in favour of the prediction. To use the language of the card-table, in the "favourable-forecast" group the trick was sometimes lost because the opponent produced an unexpected ace, but in the "dystocia-forecast" group the trick was unfailingly taken by the trump held in one's own hand, and the ace, if played at all, was played by one's partner! Further, if definite disproportion was present it could only be in very exceptional cases that uterine contractions were so strong, or head moulding so great, or pelvic "give" so pronounced that an easy spontaneous delivery could take place.

The "dystocia-forecast" group consisted of 104 cases. Of these 86 did in fact have difficult labours. Of these cases in which a wrong prognosis was given, 6 were border-line in the sense that had the head been only 1 mm. less in its bi-parietal diameter a favourable forecast would have been made. If these border-line cases are eliminated the prognosis was correct in 86 out of 98 cases.

Let us now consider the 12 cases out of the 98 in which an erroneous indication was given. Of these, 8 were judged "bad" by their failure to reach the supposed safety level on the cavity or outlet graphs only, and yet an easy delivery resulted. This is a reminder that the lower pelvis may in favourable circumstances expand and so allow an unexpectedly easy delivery to occur in cases of undoubted disproportion. This expansion of the lower pelvis is oftenest seen in multiparae; and it is pertinent to note that in no less than 5 of these

8 cases a history was forthcoming of a previous difficult forceps delivery. There now remain 4 cases out of the 12 in which a wrong indication was given. Of these the foetal head was abnormally broad in 2, so that the bi-parietal measurement gave an over-estimate of head size, and caused an unfavourable indication to be obtained from the graphs. This is a rare but seemingly unavoidable source of error. Lastly, in 2 cases a wrong indication was given for which no explanation could be found.

To summarize, it can be said that *the prediction of dystocia is surest when a fault is revealed in the brim graph.* Considerable weight should be given to such evidence. If an unfavourable feature is revealed only on the cavity or outlet graphs a considerable proportion (30–40 per cent) of moderately easy spontaneous deliveries will take place, or easy forceps delivery will be possible. To ignore the evidence of the cavity and outlet graphs would, however, be dangerous, for frequently—especially in the elderly woman—the pelvis does *not* "give", and the baby's head—especially if over 9.5 cm.—does *not* mould, and a particularly difficult delivery is then encountered. Patients showing cavity or outlet faults must therefore be looked upon as cases of "suspect-dystocia" and suitable provisions made for their supervision in labour by an experienced obstetrician.

It may be questioned whether the graphs adequately cater for all the pelvic abnormalities that may be detected on examination of the pelvic radiographs. They do not; although they do cover the major features. Among the omissions the following may be mentioned:

(1) *A high inclination of the pelvic brim.*[26] If the pelvic brim is highly inclined (that is, the brim assumes a nearly vertical position when the woman stands erect) there is often a slow start to labour and the head is late in engaging. Often
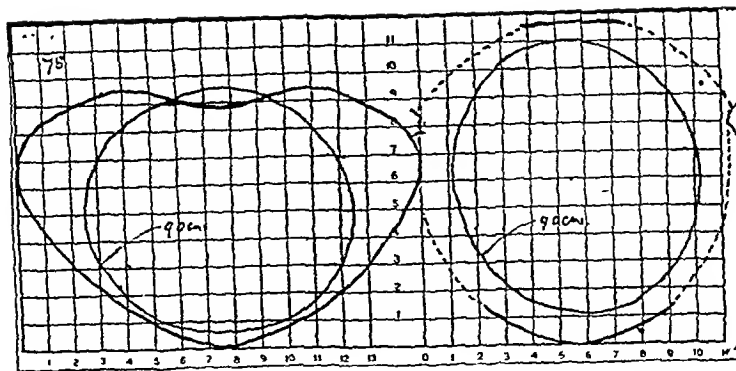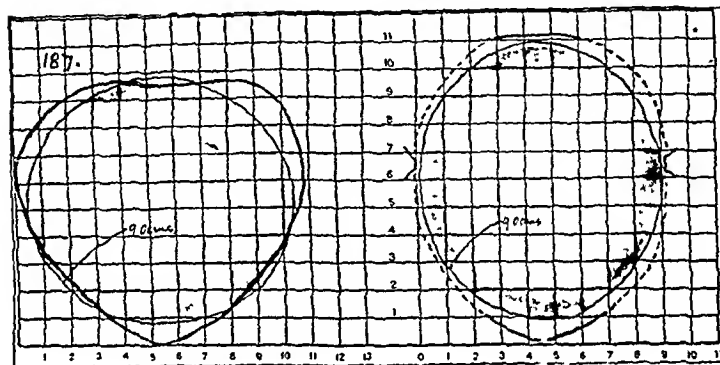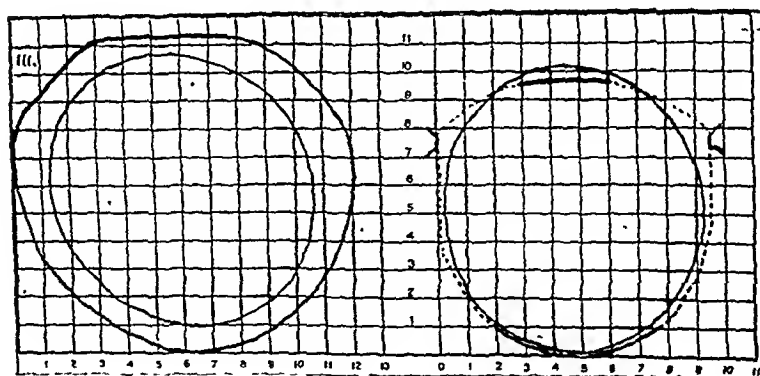
PLATE XII.

Charts showing the relationship of the flexed foetal head to the pelvis at brim level (left), and ischial spine level (right).
A. Rachitic flat pelvis.   B. Generally contracted and wedge-shaped brim.   C. Contracted outlet (funnel pelvis).

In Case A there was a long delay at the brim, but an easy low forceps delivery was later effected. In Case B Caesarean section was required (previous craniotomy). In Case C there was a long delay at the outlet and forceps delivery failed; subcutaneous partial symphysiotomy was then performed and a living baby easily delivered.

C. M.

PLATE XIII.

Hydrocephaly wrongly diagnosed.

A patient arrived with a letter stating that the foetus was hydrocephalic, and requesting that operative treatment should be undertaken   Examination of the accompanying radiograph (left in above illustration) showed that it had been obtained with the patient in the dorsal position, with consequent enlargement of the foetal head out of proportion to that of the foetal body. A second picture was obtained with the patient in the prone position, and a normal foetus revealed (right in above illustration). This patient later had a normal delivery of a healthy child.

C. M.

there is also an occipito-posterior position of the head which in certain circumstances (Fig. II) is likely to develop into an obstruction, with the occiput occupying the hollow of the sacrum and the brow pressed against the pubic bone. If therefore there is already some tendency to disproportion, the prognosis is worsened by a high inclination of the brim.

(2) *The sacrum lacks the normal full curve from above downwards*. A flattening of the sacral curve results in a lessened antero-posterior dimension of the intermediate part of the pelvic cavity (lessened posterior sagittal diameter); and if there is already a tendency to disproportion, the prognosis is correspondingly worsened.

(3) *Malposition of the head*. The significance of this complication is so obvious that it needs little comment. The head normally enters the brim in the occipito-lateral position, but any decided turning of the occiput to the posterior position, especially if combined with a sharp angulation of the long axis of the head to the long axis of the foetal trunk (Fig. II) is liable to lead to a delay in labour, and prognosis is then worsened.

A useful way of assessing the extra difficulty likely to be encountered when the above complications are found is to assume that the bi-parietal diameter measures 1, 2, or even 3 millimetres more than the estimated dimension. In the results just presented these complications were intentionally disregarded in order that the value of the graphs could be assessed apart from any adjustments or reservations on the part of the observer. Had these adjustments been made greater accuracy in prognosis would have been reached.

Since the first object in constructing these graphs was to determine whether or not they would provide a quick and convenient method of assessing the obstetric value of

the pelvis relative to the foetal head, it was desirable to eliminate as far as possible any variable or uncertain factor. To this end, the exact size of the foetal head (bi-parietal diameter) was established by clinical measurement after moulding had disappeared. Thus, as may have been gathered, the figures given are based on radiographic pelvimetry but not upon radiographic cephalometry. They therefore do not represent true ante-natal prediction. Cases in which *all* the data have
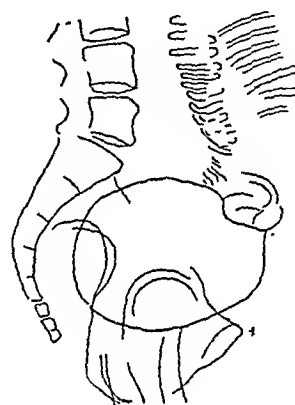
FIG. II.

Tracing of a radiograph showing arrest of the head in labour in an occipito-posterior position. The uterus is braced back against the vertebral column causing the foetal trunk to be sharply angled (extended) on the head. In the unfavourable mechanical conditions thus created progress is arrested.

been obtained by radiological means are not yet sufficiently numerous to enable an adequate test to be made, but there is reason to suppose that when that number is gathered the results will not be substantially different from the sample now given.

As a final comment on this method of reckoning the relationship of the foetal head to maternal pelvis let me again emphasize two points. This system of graphs enables the main obstetric features

to be quickly and easily evaluated, and in consequence it enables prognosis to be put on a much surer basis than is possible with "impressionistic" type of interpretation that has hitherto generally prevailed.

THE USE OF RADIOLOGY IN CERTAIN SPECIAL CONDITIONS.

Brief mention will now be made of circumstances in which radiology has been found to be specially helpful.

High head at term and suspected pelvic contraction. This topic has been thoroughly discussed. Here I would add that it is no part of my mission to belittle the purely clinical methods of examination. It is on occasions when obstetric examination is difficult, or its findings equivocal, that resort must be had to radiology.

Abnormal or prolonged labour. Intrapartum radiology has in the past been surprisingly neglected. Not only will it help in diagnosing abnormalities of the foetus, malpresentations and the like, but, more particularly, it will often explain why progress is abnormal or delayed; and by showing whether or not the greatest diameter of the head has already passed through the contracted level of the pelvis it will give material help in deciding subsequent treatment in cases of trial labour.

Post-maturity and prematurity. In these conditions, cephalometry helps to establish the degree of development of the foetus. This, however, is a subject outside the scope of these lectures. The treatment of post-maturity largely depends on the size-relationship of head to pelvis, in the diagnosis of which radiography is undoubtedly helpful.

Breech presentation. When the head cannot be gauged directly against the pelvic brim as, for example, in breech presentation, there is special reason for radiological examination. Even a slight degree of disproportion may be a serious obstacle in breech delivery, for moulding has no time to develop, and a misfit, if present, does not become obvious until it is too late to avoid disaster. It is my firm opinion that every primigravida in whom a large, or even average-sized, foetus presents by the breech and version has failed, should have the benefit of careful pelvimetry and cephalometry.

Suspected hydrocephaly. In this condition radiology has an obvious use and may establish a diagnosis when clinical examination yields doubtful results. Nevertheless, caution must be observed in interpreting the radiograph, and in borderline cases the foetus must be given the benefit of any doubt. It should scarcely be necessary to point out that, when the head lies in some unusual position, special care must be taken to guard against radiographic distortion. I have experience of more than one case in which a foetus presenting by the breech has been wrongly diagnosed as hydrocephalic, sometimes with deplorable consequences. This has happened because the patient has been examined in the dorsal position: the foetal head then projects towards the X-ray tube and casts a shadow magnified out of proportion to that of the rest of the body (Plate XIII). With the technique described in the first lecture there is no possibility of such an obvious error.

Shall the patient be delivered at home or in hospital? In recent years there has been a decided change in the attitude of the public to maternity hospitals, and these institutions are more and more being asked to provide facilities for even normal confinements. The demand far outstrips the beds available. While this is so it is also true that examples are not far to seek of women being confined at home who, as events subsequently prove, are entirely unsuited for domiciliary delivery. It may be said that such events should never happen if ante-natal examination is adequate. This is true: but at the

present time it is the supply of adequate examiners that is lacking; and it is useless to pretend that this work can be done by anyone who holds a medical degree or nurse's diploma.

From what has been said it will be realised that radiology can differentiate between those patients in whom there is every reason to expect any easy spontaneous delivery and those in whom there is definite, or possible, risk of distocia from pelvi-foetal disproportion. A strong case can therefore be made out for routine radiological examination of every primigravida who is to be confined in her own home, especially if medical help is likely to be difficult to obtain. The routine radiological examination of the lungs of candidates entering the Services may in future have a counterpart in the routine radiological examination of patients entering their names for domiciliary delivery by municipal or district midwives.

Previous difficult labour. The death of a first baby is a heavy blow for a woman and the event will sometimes cloud the remainder of her life. After hard childbirth the question naturally arises whether misfortune will again befall the patient in a subsequent delivery. Not unreasonably, a delivery by Caesarean section is sometimes demanded, although on purely obstetrical grounds there may be no indication for the operation; indeed, experience shows that difficulty in a first labour is frequently caused by disordered uterine action rather than an abnormality of a recurring nature. When faced with these questions it is often difficult to make a decision. Radiological examination of the pelvis is then a boon, for the obstetrician is placed in a much better position to decide in advance the best line of treatment for his patient. In many cases the examination will result in a dispelling of anxieties that needlessly vex the woman's mind.

The fear of obstetric difficulty. Sometimes an unreasonable fear seizes a woman and she becomes obsessed with dismal forebodings. In these circumstances radiological examination gives extra weight to clinical examination and may be the means of allaying distress and restoring courage. An amusing example may be quoted.

A young, well-to-do lady consulted an obstetrician early in her pregnancy. She was told that her pelvis was small and that a Caesarean section would be necessary for the safe delivery of her child. She accepted the verdict and made arrangements accordingly. Meanwhile, air raids started and she was forced to leave her home, eventually reaching Oxford. My colleague, the late Dr. Sturrock, examined her but could find no evidence of pelvic contraction. As the patient was incredulous, he kindly referred her to me for further opinion. I also failed to find any contraction, but also equally failed to convince the patient, who, not unnaturally, had faith in the opinion of the first obstetrician to whom she had been specially recommended. I then made a radiological examination and found that the pelvis was not merely adequate in size but that it was actually one of the largest I had ever measured. This examination finally convinced the patient that Caesarean section was unnecessary, and I later had the satisfaction of learning that she was safely delivered after a normal labour lasting only a few hours.

THREE CRITICISMS ANSWERED.

Obstetrical radiology has been criticized because it emphasizes certain features of the birth process and ignores others that also play a highly important part in deciding the course of labour. This, of course, is perfectly true, and we must always be on guard against investing radiological reports with unreasonable importance. Nevertheless, disproportion in its widest sense is chief

among the causes of difficult childbirth, and here it is that radiology gives most help. If we trouble to take pelvic measurements at all we show our belief in their value. And, if we so believe, then surely it is right to strive for fuller knowledge and greater accuracy. I have not discussed uterine function, foetal position, mental fortitude and the rest, not because these matters lack importance but because they are not the subject of these lectures.

The fear is sometimes expressed that increased use of radiology will lead to increased and unnecessary surgical interference. This is possible when bad radiology is combined with bad obstetrics. But a similar fear might equally well be expressed when radiology is used as an aid to the diagnosis and treatment of fractured bones, of alimentary disorders, of pulmonary disease and so on. Yet radiology is accepted without question as a useful and even indispensable help in these conditions. Why, then, should we boggle at its use in obstetrics when so many of our problems are essentially mechanical in nature? The fear of needless surgical intervention has little foundation in fact. In my own experience radiology has oftener influenced me against Caesarean section than it has in favour of that operation.

It is further said that an increased use of radiology will lead to a weakening clinical judgment and that the radiologist will displace the obstetrician in deciding the manner in which delivery shall be conducted. This criticism again supposes that the obstetrician has no ability or clinical judgment of his own, and again in reply it may be said that if it is true that radiology has a stultifying influence in obstetrics, then it must have a like influence in other branches of medicine, as, for example, in the diagnosis and management of cases of pulmonary tuberculosis. In point of fact the fear is groundless. The obstetrician's

clinical judgment is bettered, not worsened, by his increased knowledge and his clearer mental picture of the happenings in his patient's pelvis. And I trust that I am not expressing any disrespect for my radiological colleagues when I say that I do not suppose that they have any wish to be considered dispensers of judgment on the purely clinical aspects of obstetrics.

Finally, let no one suppose that radiology provides an easy short cut to good obstetrics. Only by sound clinical judgment can that end be reached. But sound judgment depends on the observation and appreciation of many diverse clinical features, and it is regarding one of the more important of these that radiology gives a keenness of perception unimagined by Ingleby and his generation.

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Head Flexion in Forceps Technique

BY

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THE mechanical principles implicit in the design of the axis-traction forceps, the various forms of the female pelvis, and the different attitudes and positions of the *foetal head, not infrequently supply* problems which some of us find difficult to solve even with all the available knowledge applicable to technique. It is an essential part of successful forceps technique to apply the blades to the fully flexed head and to maintain this flexion until descent reaches the level where extension becomes the normal movement of delivery. In this connexion the words of Milne Murray are worth quoting: "We may con-·sider," he writes, "the case of a normal pelvis where (for one reason or another) it is necessary to apply the instrument at the brim. Our object here is not to overcome special resistance so much as to apply a force in the appropriate direction so as to effect delivery with the least amount of that force. Our object then resolves itself into seizing the head in such a way as to develop and keep up flexion and to pull at all times in the proper axis." In the same paper he refers to the forceps as promoting flexion. It is true that the high forceps operation is not so frequently practised nowadays but it may still be the method of choice following the correction of certain malpositions. The same principles govern technique so long as the engaging diameter of the head is at any level above the obstetrical outlet and if they may sometimes lead us to a counsel of perfection which is some way removed from a similar perfection of achievement, the distance between these two ideals must always be the measure of our success.

This short paper attempts to illustrate certain aspects of flexion associated with vertex presentation which, although perhaps well known to most obstetricians, are not usually described in the textbooks, and which, while constituting some of the details of forceps technique difficult to attain in practice, at the same time comprise knowledge essential to the technician who constantly strives to perfect his own technique.

THE PROBLEM IN PRACTICE.

Most of the conditions which produce departure from the normal attitude of flexion of the head are described in the literature and need no recapitulation here. The occurrence of a median vertex presentation, the so-called military attitude, is not recognized by most authors, yet there are probably few experienced obstetricians who have not encountered it. The head sometimes lies in this attitude above the brim before labour begins and during labour, when uterine contractions are poor and the pelvic resistances slight, the deflexed attitude may remain undisturbed. In these circumstances such a head may descend in the transverse diameter of the pelvis and become arrested in the

transverse of the outlet forming a type of "deep transverse arrest," which, as De Lee points out, is scarcely to be distinguished· from arrested rotation in occipito-posterior positions. In the presence of a powerful uterine force and normal pelvic resistances, flexion of the deflexed head is probably the rule.

The following case report provides interesting data.

Some time ago there was admitted into the Rankin Maternity Hospital a woman aged 40 years, in labour. She was full time, the onset of labour spontaneous, and her doctor stated she had been having pains for 48 hours. He had delivered her on 3 previous occasions and without difficulty. Her first infant born in 1926 weighed 14 pounds, her second in 1930, 12 pounds, her third in 1934, 7 pounds. She aborted at 4 months in 1942. During each of her labours she had been difficult to control owing to intolerance of pain. On this occasion her doctor had sent her into hospital because the head was still high and the patient herself almost maniacal. On examination she was found to be an Italian weighing over 20 stones. Abdominal palpation gave no information. The vagina was extremely capacious, and the whole hand could be easily introduced without causing her any discomfort. The cervix was fully dilated except for a small anterior rim. The head was still high, deflexed but with the occiput anterior. It was mobile and the impression gained was of a very roomy pelvis. There appeared to be no reason why delivery should not be spontaneous and non-descent was considered to be due to inadequacy of uterine force. A pad and binder were applied in the hope of promoting head flexion and assisting spontaneous expulsion. Morphia and scopolamine failed to reduce her vociferous response to pain and the Minnitt's apparatus was equally ineffective. After a few hours it became obvious that delivery would have to be assisted. The capacious vagina and roomy pelvis suggested that forceps delivery would not be difficult. The hand was introduced and full flexion of the head obtained before applying the blades. The blades were applied accurately to the sides of the head and traction begun. When traction-force had reached

about 40 pounds the blades began to slip and were immediately removed. Examination found the head extended. Flexion was again obtained and the scalp over the occiput grasped with Willett's forceps. While an assistant maintained flexion by pulling on the Willett's instrument, the blades were re-applied. When traction force again reached about 40 pounds it became apparent that the head was becoming extended since the assistant was not able to maintain it in flexion against the more powerful movement of extension and the Willett's instrument tore free. At the same time the blades began to slip and were removed. Delivery was then accomplished by performing internal version and extracting as a breech. The foetus weighed 7 pounds 9 ounces and was stillborn.

EXPERIMENTAL OBSERVATIONS.

This failure to effect delivery with the forceps under circumstances which seemed to favour a safe and easy delivery was disturbing, and an early opportunity was taken to reproduce experimentally and as accurately as possible the conditions which had determined the result of this particular operation.

The head of a full-time foetus was fully flexed and fixed against very slight resistance with the occiput directly anterior. The blades of the forceps were applied along the occipito-mental diameter and traction begun. When traction-force reached about 40 pounds two things happened. Firstly the head became deflexed and secondly the forceps began to slip from the deflexed head. The deflexion of the head and the slipping of the blades really occur simultaneously, for the movement of extension raises the head from between the blades although slipping is scarcely appreciated until the head has become deflexed. Somewhat similar movements are occasionally seen when delivering the head through the vulva with the axis-traction instrument. If the rapidly-changing axis of the head is

not at the same time accompanied by a similar change in the direction of traction the blades slip from the extending head, sometimes even before the mouth and chin have cleared the perineum. In the experimental conditions it was found that by increasing the resistance to extension by narrowing the canal or by merely making pressure over the face, the traction-force necessary to effect it was raised.

DISCUSSION.

Two important facts emerge from these observations:

1. The pull exerted on the axis-traction forceps tends to deflex the normally flexed fore-coming head.

2. Maintenance of flexion is a function of the maternal resistance in the conditions governing forceps extraction.

The movement of extension is prevented by the resistance of the birth canal and as the traction-force is raised the forces distending the canal are raised more or less proportionately and chiefly because of the tendency to increase of the diameter of engagement. A moment's reflection will show that this is inevitable. The foetal head moves at the atlanto-occipital joint and the old conception of this joint representing the fulcrum of a head lever with a long anterior and a short posterior arm gives an excellent mechanical representation. When the head is fully flexed the blades of the forceps grasp the long arm and their axis lies in front of the fulcrum so that deflexion of the head is the normal response to traction-force and can be prevented only by a sufficient resistance where the ends of the lever impinge on the walls of the canal. Figs. 1 and 2.

Experience with controlled axis traction suggests that the tendency to extension

which is produced by traction-force is, in most cases, easily balanced by the counter-forces of the resistance with pulls up to about 50 pounds. As the traction-force is raised above this level the resistance finds it increasingly difficult to prevent extension, and the extent of laceration is often the measure of this difficulty. In this way we may be able to explain the difficulty and
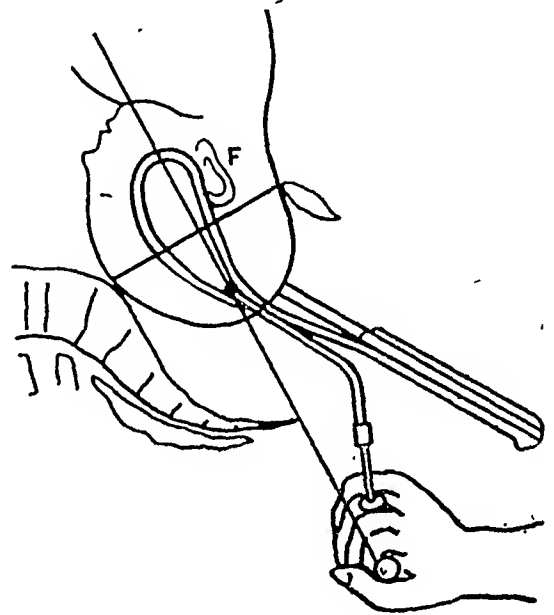
FIG. 1.

The head is fully flexed and the occipito-mental diameter coincides with the pelvic axis at the level of engagement. The blades have been applied along the occipito-mental diameter. With the fulcrum of the head lever at F, traction will tend to deflex the head.

laceration associated with forceps delivery in cases definitely without disproportion and in which the blades have been applied accurately to the head in flexion, since there is no other apparent reason why such cases should not be terminated by the use of force no greater than that of nature, and with no more injury to the soft parts than is commonly observed after spontaneous expulsion.

When the head is fully flexed, the occipito-mental diameter coincides approximately with the pelvic axis at any level from brim to pelvic floor. It follows that if the blades of the forceps are placed along this diameter as they should be in these circumstances, the direction of traction will be in the axis of the birth canal. If, however, the head deviates from full flexion, the ideal applica-
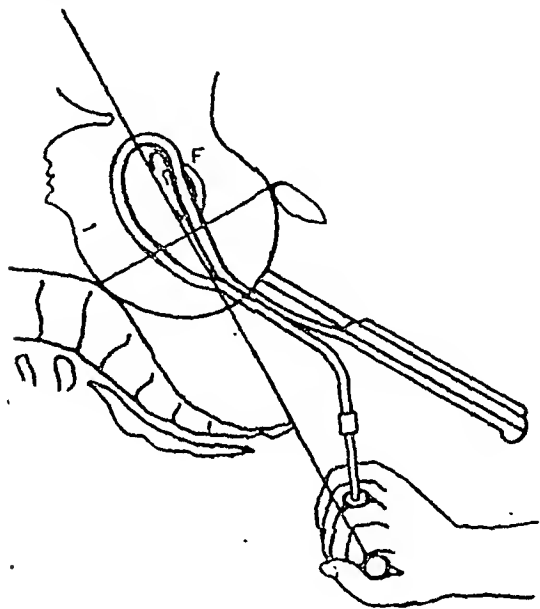

FIG. 2.

The head is deflexed. The occipito-mental diameter deviates from the pelvic axis. The blades have been applied in the pelvic axis. With the fulcrum of the head lever at F traction will tend to increase extension.

tion of the blades along the occipito-mental diameter will not promote flexion but will tend to increase deflexion when traction is begun, nor will traction-force itself be directed in the pelvic axis. When the head is deflexed, application of the blades over the ears, so that the long axis of each blade lies just in front of the tragus, while the tip reaches over the angle of the jaw, will allow traction in the pelvic axis but will also tend to increase extension when traction is begun. (Figs. 1 and 2).

It is easy enough to demonstrate the great importance of full flexion of the head in forceps technique but it is not so easy to suggest a means of obtaining and maintaining it in cases where it is wanting. As has been suggested in the case described above, the Willett's instrument is worse than useless for this purpose since it will only result in laceration of the scalp. When uterine contractions are frequent, traction-force may be made to coincide with them while at the same time fundal pressure may be useful. In this way advantage is taken of the normal flexing effects of the natural forces. It has been pointed out above that a pull greater than 50 pounds tends to increase the engaging diameter and to put the soft parts under a tension which rapidly approaches rupture as the force is raised above this. Much trouble may, therefore, be avoided by the patient development of a rhythmic traction-force up to 50 pounds, coincident with uterine contractions and, when greater force is necessary, by "stepping up" the pull slowly and gradually. It is fortunate that most cases can be delivered with a pull no greater than 50 pounds, since a greater force can only increase the difficulty of extraction and although this is eventually achieved, it is usually at the expense of the soft parts.

The late Joseph De Lee was well aware of the great difficulty of obtaining an accurate technique with the axis-traction forceps, and he strongly condemned the use of this instrument. He, himself, in the matter of forceps technique, was a disciple of Pajot. "By means of Pajot's manoeuvre," he writes, "we can give the head a direction which a knowledge of the mechanism of labour will indicate: by careful observance of the tendencies of movements which the forces of nature give the head, we can determine in which way to apply traction, and we can aid one or other as

required.'' By contrast, he states, one can only pull blindly on the Milne-Murray instrument. Despite this criticism from so great a master of obstetrical technique, there can be little doubt that the axis-traction forceps is capable of great accuracy and when it fails to achieve this the fault lies, not with instrument, but with the operator. This accuracy would be increased and the operation rendered safer if some means could be devised to maintain head flexion during traction and so ensure the engagement of the smallest possible diameter of the head in its passage through the pelvis. In this way the maternal tissues would be spared a strain which nature never intended they should support.

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A Preliminary Report on the Pelvic Brim Index

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PART I. GENERAL.*

A. *Introductory Note.*

THE purpose of this communication is to
report pelvic brim index values derived
from series of South African Negro or
Bantu pelves, and at the same time to dis-
cuss the variation of the index figures in
different races and in the same race under
different conditions.

The index is of value because, in con-
sidering the pelvis in its simplest form as a
girdle, the obstetrician is immediately
satisfied, and the anatomist accepts the
plane under consideration because it is
defined by the iliopectineal line. In its non-
pathological form this girdle is invariably
rounded or well curved laterally, and the
index gives a good practical impression
of its shape, viz. whether it is round,
transversely oval, or oval in the sagittal
plane.

The index is of interest for two reasons
in the first place. These are based on two
characteristics of the index that have been
recently discovered. First, it appears
that under favourable, healthy living con-
ditions the index—even in the same district
—can be higher than is found in circum-
stances of poverty. Secondly, the pelvis
most favourable to spontaneous labour has
proved to be the one which is oval antero-
posteriorly (index over 100). In addition

to this, it has been shown (Heyns, 1946a)
that the evolutionary purpose in man is
to produce the "anthropoid type" pelvis
with index over 100. In accordance with
Bolk's hypothesis (1925–26), the retarda-
tion of the factors leading to pelvic matu-
rity is sufficiently effective to leave the
stamp of foetalization on the majority of
adult pelves: only a minority excel,
become phylogenetically more highly
evolved, and are in fact more efficient as
ultra-dolichopellic pelves. The latter have
larger inlets, presumably because ilium and
pubis grow inordinately at the Y-shaped
epiphysis; and it is possible that in such
pelves the inlet plane has a relatively
greater area because less active growth in
this region would simply have resulted in
the smaller area of a round or flattened
brim. The causes of this hypothetical
greater acetabular than symphyseal
growth have to be discovered, and herein
lies the significance of this simple index,
for it is a good criterion of pelvic develop-
ment and growth. The pelvis, apart from
the girdle proper, is of minor interest to
the obstetrician and possibly even to the
anatomist.

B. *The brim index in different races.*

So many figures have been published on
this important pelvic index, and as in
Turner's paper (1886) so many races pro-
viding only a few specimens have had their
respective indices put on record, that it is
of value to possess Bantu figures derived

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* Part I of this paper originates from a D.Sc.
Thesis, University of the Witwatersrand.

from a reasonable series. The mode of life of the Bantu is significantly different from that of the European, and dissecting room specimens need not be considered to be selected from any particular social stratum as tends to be the case with the European. For Europeans alone, Martin (1928) and Turner (1886) collected figures for both sexes from 7 authors, of whom 3 found a higher index for the female and 4 a higher index for the male.

In the English literature the pelvic brim index is known as the index of Turner (1886) who himself, however, explains how Zaayer (1866) came to be the first· to use this valuable numerical expression. The findings for Bantu skeletal material were as follows:

that the index is over 90, and that it is, therefore, mesatipellic in Turner's (1886) sense.

The female Bush pelvis gave a brim index of 105.2, the 4 pelves studied by Orford having an index of 99, 112.6, 97.3, and 112 respectively. The male Bush pelvis has the high brim index of 97.7, ranging in 9 pelves between 88.6 and 105.5 (Orford, 1934). Slome (1929) found the average index for 2 female Bush pelves to be 99.7 and for 5 male pelves 89.2. When Turner wrote in 1886, 8 female Bush pelves and 5 male had been measured by different authors. The females showed an average index of 89, which suggests that the true mean is lower than Orford's high figure of 105.2; and the males an index of 99.5. The

Series	Mean	S.D.	Range	Significance: Difference of means ÷ Standard error of means		
65 Female	90.35 ± 1.02	8.20	69.6 — 104.4			
50 Bantu	92.80 ± 1.34	9.47	70.2 — 117.0	1.17	0.88	
50 Zulu	91.08 ± 1.17	8.24	75.5 — 110.0			
100 Male	91.56 ± 0.91	9.11	70.2 — 117.0			

The index values in 100 Bantu primigravidae ranged between 79.7 and 121.2, the mean being 93.6 ± 0.72 and standard deviation 7.2. The number (i.e. percentage) of indices 100 or over was 17, which corresponds closely with the figures for the skeletal material of both sexes. These measurements were gained radiographically with the brim parallel to the film. In a second series of 25 non-pregnant women X-rayed by Nicholson's (1936) stereometric technique, the mean was 91.27. The application of this index in X-ray pelvimetry is discussed elsewhere (Heyns, 1946 b).

It can now be said that the Bantu male has an index comparable with that of the female, and that there is no significant difference whatsoever between the sexes;

male indices ranged from 93 in Fritsch's (1872) specimen to 109 in Turner's. Thus the total of 19 male pelves give a dolichopellic index, or one over 95. The females appear to have a lower index.

It is important now to consider whether a flattened or rounded brim is to be expected under favourable living conditions, and what is the evidence for the belief that the European trend is in the direction of the round brim with index near to 100 (Thoms, 1941; Ince and Young, 1940; Nicholson, 1945).

Authors of last century found strikingly low indices. Thus Turner (1886) and Verneau (1875) amongst others found average indices below 80 for the higher races. In many cases small series of under 20 specimens were reported on, and Verneau

himself studied biometrically only 35 females and 63 males amongst European pelves. It is difficult to account for these low indices, even if different measurements were employed for conjugate and transverse diameters which, in the majority of cases, have termini that are well marked on the bones.

For a living racial group, one of the lowest indices found was the value (81.8) derived from Pan's figures (1929) for 64 Hindu females. By comparison, only 16 of the 100 male Bantu pelves had an index below 82. An index of 80 or 81 to-day as an average for white races seems extremely unlikely, though it has to be confessed that this opinion rests on the precarious information derived from radiography. Nicholson (1938) found a mean of 88.3 for the brim index in 350 rural English women, and Ince and Young (1940) a mean index of 90.8 in 509 London women. Thoms (1941) who consistently fails to report averages for the indices of which he frequently publishes other analyses finds that the great majority of his American subjects have an index of over 90, and that a minority are platypellic. Greulich and Thoms (1939) have even brought evidence to suggest that a group of 104 nulliparous students of superior economic and physical status has a mean index which is dolichopellic. In the light of this evidence, and from findings in the Bantu—and even in the dolichopellic Bush race—the prevailing belief that the platypellic type of brim is characteristic for the female is not well founded. Jarcho (1933) believes that the round or dolichopellic type of pelvis is found in the aborigines of America, Australia, and the East Indies; and at the other end of the scale there is the view (Stoney, 1930; Vaughan, 1937) that platypellic pelves are less the result of racial influence than of the conditions of life in modern civilization.

In his stimulating paper Derry (1923) bases some conclusions on his pelvic chilotic line which corresponds with that portion of the iliopectineal line extending from its anterior extremity on the ilium to the sacro-iliac joint. It was found that females of the Sixth to Twelfth Dynasties possessed pelves with the greatest antero-posterior diameter. English hip-bones from Whitechapel indicated smaller pelves in this respect than even the Predynastic and Kerma (Nubian) innominate bones studied. The English material was thought to be less typically female than is the case in Egyptian women generally, and even less so when compared with the women of the Sixth to Twelfth Dynasties. Because the Predynastic and Kerma female material was less differentiated from the male than was the case with the corresponding higher English and Old Empire groups, Derry sees confirmation of the view that there is less sex differentiation in primitive than in higher races. Kenny's findings (1944) show how correct was Derry's conclusion that a large antero-posterior diameter is of greater importance for an easy labour than a large transverse.

Two interesting racial groups are the Veddahs of Ceylon and the Indians of Pecos Pueblo. While the former gave an index (Hill, 1941) of 91.9 (13 males) and 91.2 (7 females), the corresponding Indian figure was below 74 in all female groups (Hooton, 1930). The Pecos Indians subsisted chiefly on maize, and there is evidence that the health of the inhabitants declined during the closing periods of the settlement. Nevertheless, the female brim index was 70.5 in the two earliest periods, and the male remained approximately the same throughout (mean 76.1). These pelves were extremely wide, both at the brim and the iliac crest, as compared with the Bantu, and the brim calculated mean area of 95.5 sq. cm. compares with the

corresponding female Bantu figure of 101.2 sq. cm. The Pecos area is similar to Pan's (1929) for the female Hindu (95.1 sq cm.), yet the latter has a brim transverse of the same order as the Bantu female. The Pecos superior strait is, therefore, much flatter than that of the Hindu which in turn is considerably flatter than that in the Twentieth-Century Bantu, English, or American white female.· The Veddahs show an index equal to that of the last three groups. This Ceylon race availed itself of a range of food which is almost unequalled, an exception being the absence of milk. Hill (1941) states that water was the only drink known to these people. As milk is the only rich source of calcium, it is difficult to understand how in the Veddah rickets is avoided during childhood, and consequently a flat pelvis. In many hundreds of human pelves studied, the non-rickety platypelloid pelvis of Caldwell and Moloy occurs in only 1 or 2 per cent (Caldwell and Moloy, 1933; Heyns, 1944; Kenny, 1944, etc.). There is no doubt that development of the pelvic brim during childhood and adolescence must be studied with greater precision before the factors influencing pelvic shape will emerge. The alternative view that · the morphology of the brim is due to racial factors is as unsatisfactory as postulating nutritional causes in all those cases which do not exhibit frank rachitic pathology.

Finally, the influence of sacral breadth on the brim index must be considered. The Veddah sacral index was dolicho-hieric in the male and only 100.7 in the female. Such a narrow sacrum is unusual, but has the effect of decreasing the brim transverse diameter and accordingly raising the brim index. Conversely, the female Pecos sacral index was very high at 114.3—male index 111.2—and the sacral breadth was 114.34 mm. in 47 females and 115.8 mm. in 66 females, as against a figure of 106.6 mm.

in the Bantu female. It is evident that the sacrum must be partly responsible for the low Pecos brim index. It is submitted, therefore, that the sacral breadth should always be shown with the brim index.

C. *Ontogeny and phylogeny.* .

(a) *General.*

In the foetus the brim index has been found to be over 100 just as frequently as in the adult. Thus in the Bantu 17 of 100 foetuses had an index over 100, none being exactly 100. Of Fehling's (1876) 130 foetuses available for this analysis, 12.3 per cent had an index of 100 or more. Kappers (1938) found only 2 brim indices over 100 in 53 foetal pelves. No significant sexual differentiation was found except by Fehling (1876) who was unable, however, to substantiate his claim in this respect.

In the postnatal years the brim becomes round and even ultra-dolichopellic (see Fig. F12). In the measurement of dry pelves, as Kappers (1938) pointed out, shrinkage with distortion is most marked up to the age of 7 years, and the result of this is an increase in the conjugate and a decrease in the transverse diameter· But in formalin-preserved and fresh specimens the preponderance of conjugate over transverse is still pronounced, and even after the tenth year this ratio holds. In spite of the arguments surrounding this problem, therefore, the index is in all probability higher during childhood than during the foetal period.

Veit (1883) found in 50 neonatal pelves that the ratio of conjugate to transverse was as 1 is to 1.093, thus showing no change from foetal mesatipelly. Only 3 of his own 27 pelves had an index over 100. Merkel (1903) observed an increase in the conjugate during infancy as had Kehrer (1873) before him, and Jürgens (1891) with his valuable series totalling 43.

Fig F12 Kappers' Data
BRIM DIAMETERS DURING ONTOGENY

○——— CONJUGATA VERA
×····· TRANSVERSE OF BRIM
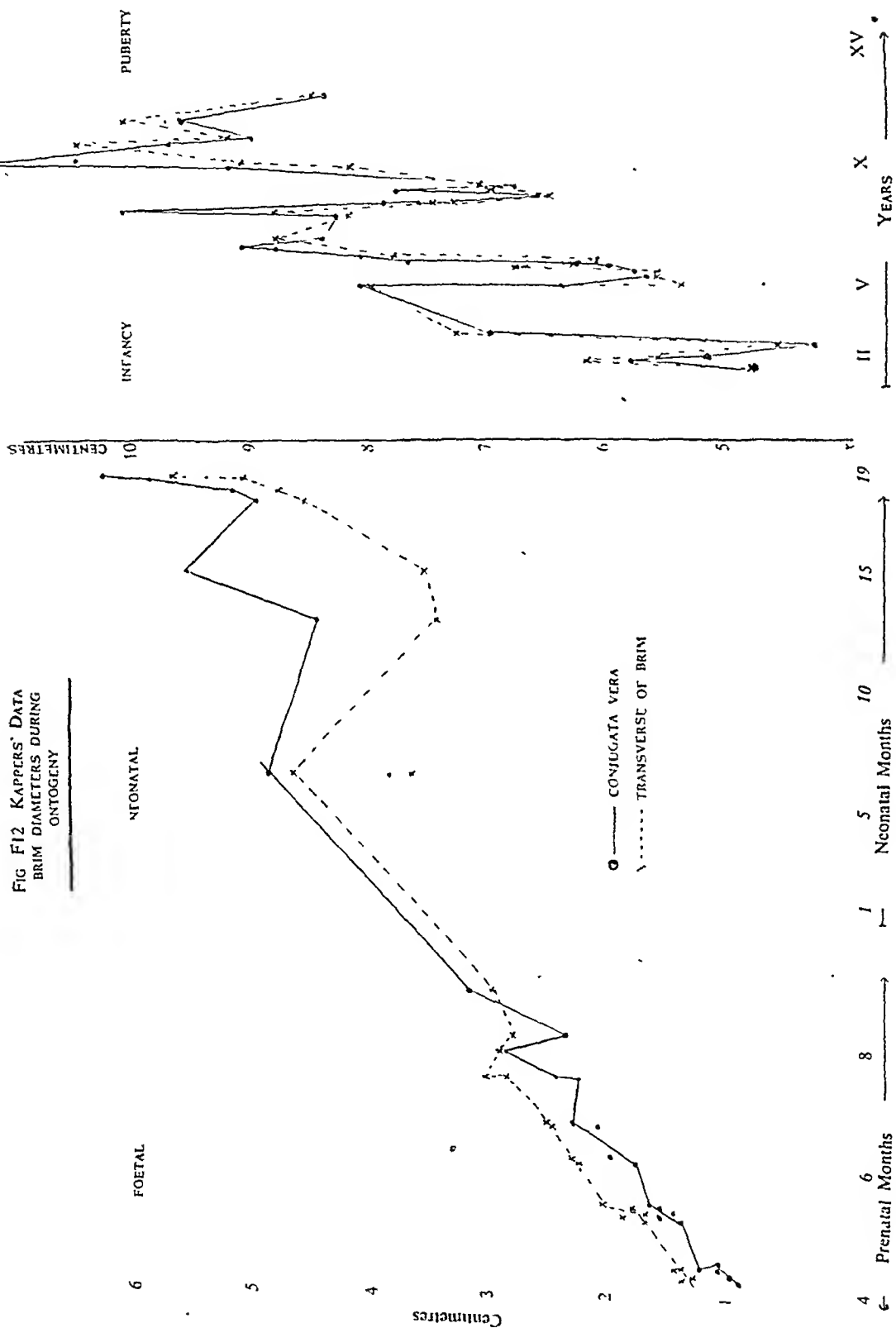
Hennig (1880) measured 5 female pelves (aged 6 months to 8 years) of which the inlets were round, and made a remark about the 8-years old pelvis that it was round while *in situ* in the fresh cadaver. A female pelvis aged 10 years was dolichopellic and Hennig states that the index is higher in children than in neonatals. In Turquet's series (1884) of 70 infantile pelves, the sagittal was equal to or greater than the transverse in 28.5 per cent. He mentions as a cause of this finding tuberculosis and syphilis, diseases to which these infants succumbed !

Breus and Kolisko (1904) state that the transverse diameter becomes less than the antero-posterior from 8 to 11 years. "It should be observed," says Kappers (1938), "that this surely cannot be regarded as unusual, when even before the 8th year a similar ratio is found." Breus and Kolisko suggest that from 8 to 11 years sacral growth is arrested with the accompaniment of a more rapid tempo in ilium growth. After this age-period, growth of the sacral breadth gains momentum and exceeds that of the ilium. But these authors measured very small numbers of children's pelves, and of these only a small proportion were young ones.

A consideration of the later phases of ontogenetic development of the pelvis must include reference to Ssoson-Jaroschewitz (1925) who studied a large collection of skeletal material. Of 150 adults over the age of 25, 13.3 per cent had an index of over 100; of 108 pelves of all ages up to 25 years, 39.1 per cent had indices over 100. The Bantu females of the present series had 13.4 per cent of anthropoid pelves (Caldwell and Moloy classification, 1933) in which the brim index is usually over 100; and of the 100 males 16 were anthropoid. This corresponds well with the Russian findings of Ssoson-Jaroschewitz (1925) and even with the 215 American (11.6 per cent)

classified by Caldwell and Moloy (1934). It is submitted that 12 per cent of the pelves of a given population can be expected to be anthropoid, and Kappers' criticism (1938) of the Russian results is not well substantiated. The fact that emerges from the Russian material, however, is that childhood shows more high indices than the adult stage.

Summarizing the position, it may be said that (1) the foetal pelvis tends to be platypellic with, towards the end of intrauterine life, occasional examples of mesati- and dolichopelly; (2) during infancy and childhood up to the age of 13 years the brim is mesatipellic: while dolichopelly is normal and common, platypelly is now rare; and (3) after 13 years and during the adult stage the pelvis again tends towards platypelly. At no period can any sexual differentiation be based on the pelvic brim index.

A phylogenetic survey shows (Schumann, 1915) that at the gorilla stage the contour of the pelvic inlet is oval, the antero-posterior diameter still being greater than the transverse, though the proportion is much more nearly equal than in any lower species. In the kangaroo the pelvic brim has the shape of a narrow triangle. The triangular form becomes progressively widened as the scale is ascended until, the sides becoming more and more concave, the brim becomes ovoid in the ungulates. In all quadrupeds the antero-posterior is greater than the transverse diameter. The infantile pelvis, then, more nearly approximates the quadruped type, and is not dissimilar to that of the highest apes.

In mammals, from the monotremata right up to the primates, there is extension of the head on the trunk during parturition (Schumann, 1915); but in anthropoid apes and man the facial angle rises above 45 degrees, and flexion of the head during birth becomes the ideal.

(b) *Bantu data.*

An ontogenetic survey of the Bantu pelvic brim has been published elsewhere (Heyns, 1946), and demonstrates the following facts.

(1) Seventeen of 100 foetuses had an index over 100 (or 100 and over); 33 per per cent were dolichopellic (index over 95).

(2) In 39 children aged 1 to 15 years, 15.4 per cent have indices over 100 and are of well-marked anthropoid type. But 35.9 per cent (14 pelves) have an index of 100 or more.

(3) (a) In 45 adolescent females aged 15 to 19 years, 13.3 per cent had indices of 100 or 100 and over, and 28.9 per cent were dolichopellic.

(b) Of 31 females aged 20 to 25 years, 19.3 per cent had indices of 100 or more, and by some chance 48.4 per cent were dolichopellic.

(c) For adult indices of 100 or over, there were 17 of 100 male dry pelves, 12 per cent of 67 female dry pelves, 17 of 100 female X-rayed subjects, and 20 per cent of another series of 25 X-rayed women. The dry pelves exhibited the Caldwell and Moloy anthropoid type in 13.4 per cent of females and 16 per cent of males, both figures being very close to those given above (12 and 17 respectively).

Concerning the foetal brims mentioned under (1) above, the index reached 110 on only two occasions, and the brims never resembled the pronounced "anthropoid type" seen in the adult: they certainly do not approach the relative proportions of the ape brim. These high-index foetal brims are in fact only round, or "more round" than the average brim.

The infant and child pelvis moves further in the direction of "roundness" than the foetal with a percentage difference which is 2.23 times its standard error. Now for the first time do outspoken "anthropoid types" appear—but the outstanding observation concerning the infant brim is the trend from flatness to roundness.

The percentage difference of indices 100 or over between the 1 to 15 and 15 to 19 year age groups is 2.5 times its standard error, and is probably significant. It is seen, therefore, that from infancy to puberty or thereabouts pelves are significantly less flat than those in the foetus on the one hand and those in the adolescent on the other. The figures for this adolescent period show no significant difference from the total figures for the age period 15 to 25 years; nor do the figures for the 15 to 25 year period differ significantly from the corresponding figures for the adult skeletal material.

The difference in the incidence of dolichopelly in the 15 to 19 and 20 to 25 year age groups is only 1.7 times its standard error, and is not significant. Similarly, the difference in the dolichopellic incidence between the foetal and the 20 to 25 year groups is only 1.5 times its standard error. Adult and foetal incidence of this character correspond closely, being respectively 34.5 and 33 per cent; and the adult dolichopellic incidence is equally similar to that of the 15 to 25 year age group.

In the adult there occurs on the average a flatter pelvis than in the child. The "anthropoid type" incidence is still equal to that in the foetus, though the "anthropoid" appearance reaches greater emphasis in the specimens so characterized. Something happens at pubertal age to arrest the development of round or ultra-dolichopellic brims, but the basis of this is not evolution (Heyns, 1946). The cause may be some combination of factors concerned with sex hormones, the influence of nutrition on metabolism, and physical forces based on weight-bearing and progression.

PART II.

ANALYSIS OF ANATOMICAL OBSERVATIONS.

A. *Testing of the validity of certain current hypotheses.*

1. Nicholson (1945), in an attempt to place the conjugata vera in the forefront of the picture, has drawn attention to the fact that the coefficient of variation of the transverse diameter is 5.8 per cent as against 7.8 for the conjugate. It is difficult to see how he reaches the conclusion from this that pelvic capacity tends to be a function of the conjugate diameter only. In 100 Bantu dry male pelves the coefficient figures were 7.1 per cent (transverse), and 10.2 per cent (conjugate); in 66 Bantu dry female pelves the corresponding figures were 6.5 and 7.6; and in 100 pregnant Bantu 6.9 and 7.7.

2. How close is the relationship between brim index and brim area ? In other words, can all brims with index over 100 be expected to have a large area and vice versa ? While it seems likely that this is the case, important exceptions have been found in the Bantu, and on clinical grounds these fall in the small category of pelves which *per se* cause dystocia. Thus in 125 Bantu women X-rayed—100 unselected consecutive primigravidae and 25 parous women who had sustained vesico-vaginal fistula—there were 4 pelves, 2 from each group, that had the cavity plane area below 80 sq. cm. The brim indices ranged from 102.1 to 109.3. The mean of this cavity area for the 100 primigravidae was 93.75 sq. cm. Thus about 3 per cent of the pelves were anthropoid types with greatly contracted girdles.

The coefficient of correlation between brim index and brim area in 100 Bantu dry male pelves was +0.256±0.1004. As $r = 2.56$ times its standard error, the relationship is only possibly significant. The correlation coefficient in 51 Bantu dry female pelves was +0.798±0.141 which is 0.57 times the standard error. In the latter instance the value of r has no significance, and bears out statistically what was suspected from the data derived from the clinical material mentioned above.

3. A third point, concerning antero-posterior flattening of the brim, needs clarification, though the evidence available is insufficient for a final solution of this aspect of the problem. If the perimeter of the brim is c cm. and the area enclosed by the brim when circular in shape is a sq. cm., then any compression of the brim causing a flat shape which is no longer a circle would result in a brim area which is less than a sq. cm. The circumference of the flattened circle would still be c cm. Whether this flattening process ever enters into the matter of brim development must now be considered.

Imagine an adult pelvis with round brim. In the early stages of osteomalacia the brim may become compressed antero-posteriorly, and there would be a loss of area. Whether rickets acts in this manner is not so easily determined. It is possible that, in addition to flattening during infancy and childhood, there is a measure of arrest of pelvic growth at the brim. Such an arrest may affect both the sacrum and the epiphyses related to the brim, or only some of the epiphyses. It is necessary to bear in mind that at the age of 3 or 4 years the pelvic girdle is quite small, and that such an increase in its perimeter occurs after this age that the girdle becomes 3 to 4 times as large in area during adolescence as it was during infancy.

If the antero-posterior compression occurring in the presence of rickets is applied to a fully, or nearly fully, developed pelvis, the abnormal bending of the bone may occur anteriorly in the region of the superior ramus of the pubis or posteriorly in relation to the iliac portion of the ilio-pectineal line. If the latter were

to occur, shortening of the conjugate diameter might well be associated with increase in the transverse diameter of the brim. Nicholson (1945) refers to this and states: "in the true rachitic pelvis there is undoubtedly a shortening of the conjugate diameter associated with a lengthening of the transverse, and it is a common fallacy that this strong negative correlation persists in the healthy pelvis." When he goes on to say that "it is obvious that this false reasoning can lead to some absurd conclusions," one is in sympathy with him. But the matter is not quite obvious, and any statistical predictions must be checked experimentally, which here amounts to precise clinical observation.

It would be of great value if workers in an industrial area where rickets is rife were to make X-ray studies of pelves showing unequivocal rickets. The necessary evidence is not available at present. In the Bantu, rickets, though common, is not often seen in severe form. Whether flat Bantu pelves with low brim indices were rickety could not be determined even when skeletal material was studied. It is possible that a rachitic pathology was the basis for flatness in these specimens, except in the cases where Caldwell and Moloy's platypelloid type was diagnosed.

(a) There is no doubt that there must be a very high correlation between · the anterior straight breadth of the sacrum and the greatest transverse diameter of the brim. It was pointed out in connexion with the Veddah and Pecos brims that sacral width played a major rôle in influencing the brim index. Against the brim index we may, therefore, consider the conjugate-sacral index which has conjugata vera as numerator and sacral width as denominator. This index should show a high relationship with the brim index. In 100 male dry pelves $r = +0.804 \pm 0.1$, r thus being 8 times its standard error and

consequently highly significant. In 61 female dry pelves $r = +0.813 \pm 0.109$, r being 7.47 times its standard error. This relationship shows that the transverse diameter is to a great extent determined by sacral width. To what extent sacral growth is influenced by rickets is not known, but it is obvious that a knowledge of this is requisite to an understanding of the effect of rickets on brim shape.

Fig. 1 shows how closely the brim index follows the conjugate-sacral index in 61 dry female Bantu pelves.

(b) The difference between the Bantu means of the brim transverse diameter and of sacral breadth is as follows: in 100 male dry pelves 8.2 mm., and in 66 female dry pelves 13 mm. The coefficients of variation were respectively 7.1 and 6.8 per cent for the male diameters, and 6.5 and 6 per cent in the females. It was found that the mean sacral width was greater in the female than the male by 2.2 mm., the difference being only 2.12 times its standard error and thus only possibly significant. The transverse diameter of the brim showed a highly significant sexual difference of 7 mm. which was 5.65 times its standard error. In order to discover whether low brim index pelves, in the hypothetical flattening process due to rickets, exhibited an increase in the transverse diameter of the brim, a simple graph was made (Fig. 2). Only differences of 15 mm. and more between sacral width and transverse diameter were recorded for this purpose. It is easily seen that if antero-posterior shortening of diameters in rickets is associated with bulging out at the iliac portion of the ilio-pectineal line, then the difference between transverse diameter and sacral breadth must be greater than in the non-rachitic pelvis. The rachitic pelvis, by virtue of becoming flattened, has a low brim index and, therefore, if rickets causes this increase in the transverse that Nicholson
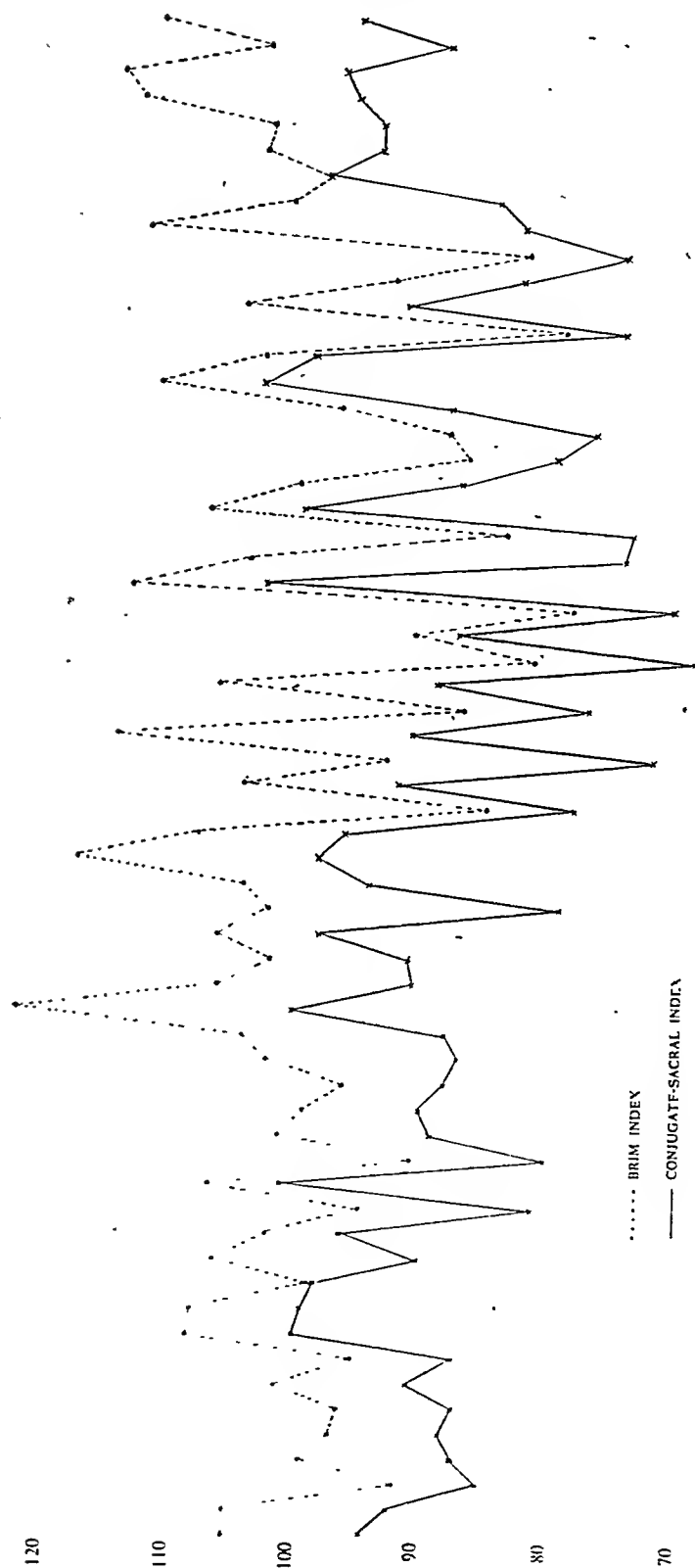
FIG. 1

BRIM INDEX

CONJUGATE-SACRAL INDEX

120

110

100

90

80

70

claims, low brim indices should be found associated with great differences between brim and sacral width. The graphs in Fig. 2 show that this is by no means the case.

It will be observed that only 16 of 100 males have the brim-transverse-sacral breadth difference 15 mm. or more, whereas 24 or 36.4 per cent of females show such a difference. It would be invalid to ascribe the greater lateral bulge of the iliac portion of the brim in the female to rickets, because there is no evidence to show that rickets affects the female pelvis more than the male. This greater bulge is a sexual character. The sexual difference in the percentage incidence of the greater bulge is significant, being 3.3 times its standard error.

In the female series of 65 pelves the mean brim index was 90.35 and the mean index for the 24 female pelves shown in Fig 2 is 88.6. The difference is not significant, it being just less than its standard error. In the male series of 100 pelves the brim index was 91.56, and the 16 male pelves of Fig. 2 have a mean index of 85.9. The standard error of the difference between the two male means is 4, and this difference is accordingly not significant. Thus brim indices should not be expected to be lower in those pelves with a pronounced difference between the transverse diameter of the brim and the breadth of the sacrum than in those with a small corresponding difference. It must, therefore, be admitted that pelves exhibiting a moderate degree of rickets do not possess a marked difference between brim transverse and sacral breadth, for rachitic pelves tend to have a low brim index value; and here it is seen that the pronounced differences occur in association with brim indices that do not differ significantly from those of the total series in both sexes.

It may be contended that the Bantu pelves used for the above argument were not subjected to rachitic influences. If that

D

is so, then Nicholson's point about the absence of a strong negative correlation between conjugate and transverse diameters in the healthy pelvis has been proved adequately. It still remains to be proved, in that case, that this negative correlation exists in frankly rachitic pelves. To the student of the ontogenetic development of the pelvis, gross deformities of the girdle due to rickets are of negligible interest because these are observed in only a few localities; but the unobtrusive effects of rickets must be observed and analyzed because of the belief that in non-industrial European communities development of the pelvis in the unequivocal absence of rickets is possibly as rare as the incidence of gross rickets. The above analysis leads to the conclusion that flattening of the brim in rickets, so far as the limits of the ilio-pectineal line are concerned, is probably confined to a bending at the brim of the pubes rather than the ilia.

B. *Factors influencing the brim index.*

What are the anatomical factors that influence the brim index? These factors appear to be as follows:

I. Growth of bone at certain epiphyses:

(a) Acetabular epiphyses, but more directly the anterior limb of the Y-shaped epiphysis.

(b) Epiphyses at the symphysis pubis.

(c) Sacral epiphyses concerned with growth in width in the region of the sacro-iliac joint.

II. Development of the sacral alae causing greater anterior curvature of the sacrum, and thus a pushing of the sacrum posterior or the rest of the girdle anterior.

III. (a) Bending, possibly due to rickets, of the bony girdle at the iliac portion of the ilio-pectineal line. This will increase the length of the greatest transverse diameter of the brim.

Fig 2
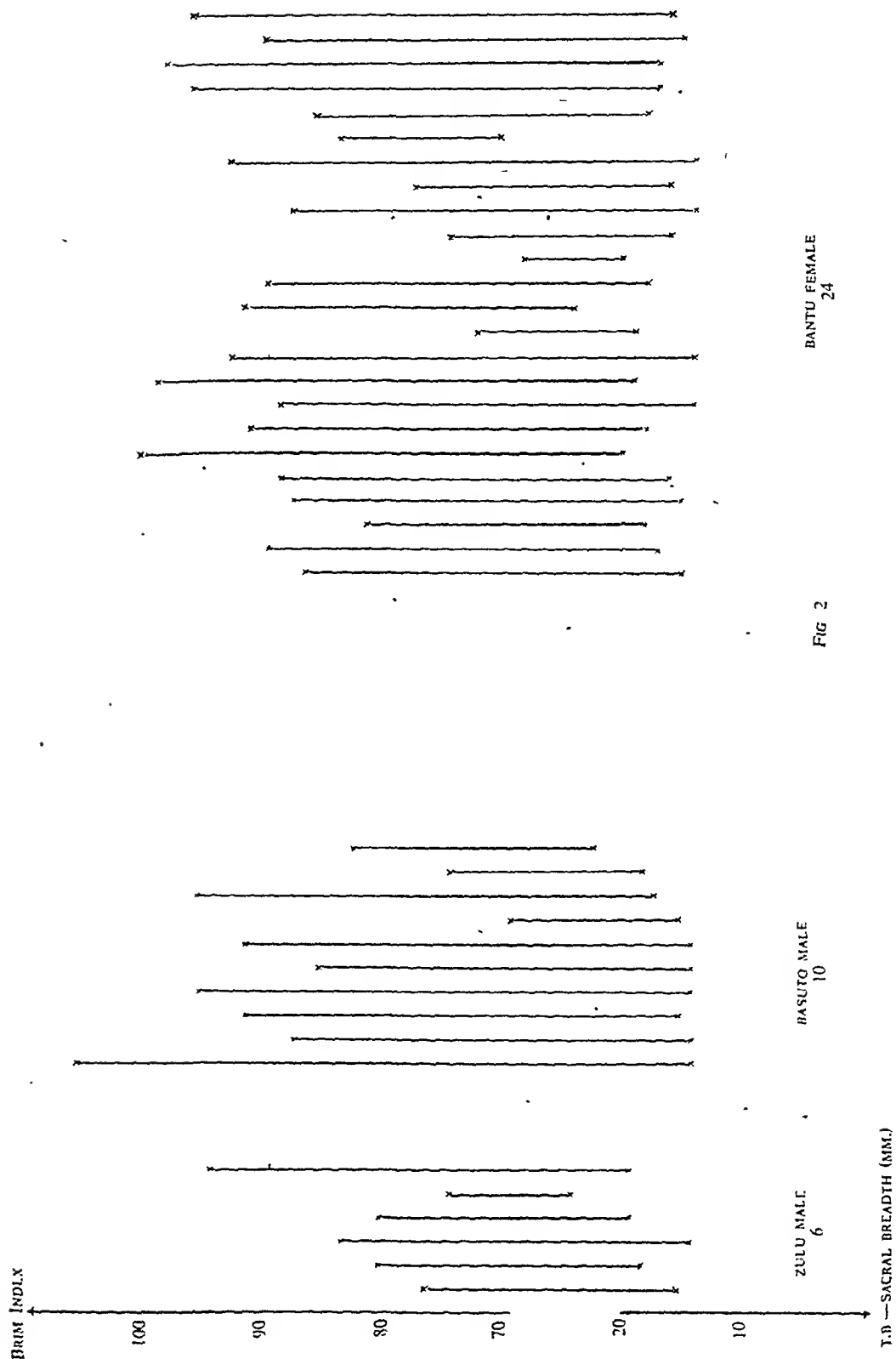
(b) Wherever the bending of bone mentioned in III(a) occurs as the result of an antero-posterior force, the conjugate diameter will be diminished.

IV. The tendency of the sacral promontory to be situated forward, i.e. near to the greatest transverse diameter, in pelves of the android type.

IA. *Bone growth at epiphysial cartilages.*

1. *Mechanism.*

If a little thought is given to the manner in which the pelvic girdle increases in size, it will be realized:

(i) That increase in antero-posterior length can only occur appreciably as the result of growth at the anterior limb of the Y-shaped acetabular epiphyses on either side.

(ii) That increase in transverse width may occur by growth either at the sacrum or at the epiphyses in relation to the symphyseal face of the pubis on either side. That the latter growth is possible no one will deny, but that growth at the symphysis is considerable will be shown to be highly probable. In this connexion reference must be made to the work of Todd (1921–23) who has traced phyligenetically the fate of the symphyseal median bar with its upper and lower nodules. This is the typical Eutherian arrangement at the symphysis pubis. Todd's observations both in Eutheria and in his extensive human material lead to the conviction that growth activity at the symphysis pubis is pronounced and, in fact, that changes in the face and certain parts in close relation to it continue right into the fifth decade of life. There can be no hesitation in agreeing with him that "the epiphysial remnants of the human symphysis, namely ventral rampart, upper extremity and to a less and more variable extent the lower extremity are the homologues of median bar and upper and lower nodules of typically Eutherian metamorphosis."

The fact that the brim index shows a pronounced tendency, from the time the infant walks, to reach values of 100 and more suggests that weight-bearing and increased mechanical stimulation of the acetabular epiphyses are associated with augmented proliferation of cells of the Y-shaped epiphysis. From Bantu data of the brim area in children (radiographic) and foetuses a calculation, on a three-dimensional basis, shows relative growth activity to occur as shown in Table I. It may be taken broadly that the 3-months-old foetus has a brim area of 0.5 sq. cm., the newborn area being 10 sq. cm., that at 2 years it is 20 sq. cm., at 8 years 50 sq. cm., and at 14 years 80 sq. cm.

The values for the different ontogenetic periods give a measure of the relative increase of bone volume during the periods under review. The active proliferation of cells during the foetal period is followed by considerable slowing down until the infant is 2 or 3 years old; after this age the individual years show a pronounced drop in activity so that the relative increase from 2 to 8 years is about one-third of the infancy period; and finally, from 8 to 14 years the rate of growth is 56 per cent of that in the previous 6 years.

2. *Increase of brim axes during ontogeny.*

What can be learned from an analysis of the two axes of the brim during ontogeny up to the age of 14 years?

During the last 6 months of foetal life both conjugate and transverse diameters quadruple themselves, the conjugate on the average being a little less than the transverse. The average brim index happens to be mesatipellic.

From birth to 2 to 3 years of age, both diameters increase by $1\frac{1}{2}$ times their length, and thereafter by progressively smaller

TABLE I.   PELVIC GIRDLE.

A Measure of the Relative Increase of Bone Volume and Length During the Periods Under Review.

Ontogenetic phase	Volumetric Vol. increase ÷ Vol. × time increase	Perimeter	Linear Sacral breadth	Conjugate diameter
Second foetal trimester	40.0			
Second and third trimesters	13.8	5.88	4.2	6.2
Infancy until 2 or 3 years	1.06	.0.21	0.13	0.17
Infancy until 2 years (Kappers' figures, 1938)	1.27			
Childhood: 2 to 8 years	0.32	0.1	0.06	0.1
Childhood: 8 to 14 years	0.18	0.05	0.04	0.05
Puberty to end of ontogeny Female	0.03	0.02	0.03	0.01
Male	0.004	0.01	0.02	0.002

factors. But after infancy the axes no longer increase pari passu. Thus during infancy the conjugate grows 17 mm. and the transverse 20 mm. In the next 6 years the conjugate grows 29 mm. (or possibly even more) and the transverse 23 mm. From years 8 to 14 the conjugate grows 23 mm. and the transverse 20 mm.

Thus from birth to 14 years the gain in conjugate length is 69 mm. and in transverse length 63 mm., the former outstripping the latter most effectively during the 2 to 8 year age period. After puberty, however, the transverse diameter takes over the ascendancy, as the following figures show.   The difference between pubertal and adult values is shown.

Male: conjugate 1.3 mm., transverse 12.6 mm.
Female: ,,   5.6 ,,   ,,   19.6 ,,
Average: ,,   3.5 ,,   ,,   16.1 ,,

Sacral breadth increases are shown in Fig. 2.

From the above data, then, it is seen that in the postnatal individual there is a very active growth period from birth to the age of nearly 3 years. Secondly, relative activity at the acetabular epiphyses varies during ontogeny in such a manner as to produce at its beginning and at its end

(i.e. from the time of adolescence) brims of a low mesatipellic order; but during childhood there is increased growth at these epiphyses which makes the conjugate axis predominate sufficiently to give, on the average, a dolichopellic brim. It is after puberty that the female transverse diameter outgrows the male, even when sacral width is subtracted, and thus causes the iliac bulge which has been ascribed to rickets.

3. *Rickets.*

Concerning rickets it may be supposed, in the present absence of further evidence, that the disturbance it causes in bone growth must be restricted to an influence on endochondral ossification, and this mainly at the acetabulum; and that it is probable that the Y-shaped epiphysis suffers over a period which exceeds the duration of florid rickets, when the latter is judged by general clinical manifestations. At the symphysis pubis anteriorly and the sacrum posteriorly, there are too many muscular and weight-bearing forces respectively to allow their related epiphyses to become unduly involved in the rachitic pathology of even the seriously immobilized child.

It is submitted that it is a mistake to think

that the rachitic effect on the girdle is associated with an actual bending of bone. Such bending occurs only very rarely at the diaphysis of long bones where distortions are due rather to irregular endochondral ossification. The exaggerated rachitic curvature of the lower half of the sacrum is not comparable to what is being considered here; and it must be emphasized that the evidence available is in conflict with the hypothesis in respect of which there is visualized an osseous softening of the girdle accompanied by some degree of antero-posterior collapse. A study of outstanding value by Dunham and Thoms (1945) throws some light on the ultimate fate of the pelvis of the child suffering severe rickets. Ten individuals who had had "the most severe and prolonged type of rickets occurring in early childhood" were re-examined in adolescence. Of the 10 adolescents Thoms considered that only 5 had rachitic pelves, though it must be denied that any unequivocal stigma of the disease is present in the only inlet roentgenogram he shows of the latter group. It is to be noted, however, that florid rickets may leave no recognizable trace in the adolescent pelvis. Is it justifiable, in the light of this and other evidence here produced, to speak as freely as is the custom of the effects of malnutrition on pelvic development? It is unusually difficult minutely to study rachitic processes as they affect the young pelvis.

IB. *Individual variables and their relation to the brim index.*

Having outlined the morphological effects on the brim of growth at the various epiphyses, it is now necessary to examine individual variables and their relationship to the brim index. For this purpose pelves will be divided into two great groups—those with index under 90 and those with index 90 and over. The objective is to discover whether the former, unfavourable group exhibits dimensions which are also unfavourable in the functional sense; and secondly to ascertain which irregularities of growth cause the low brim index.

1. *Brim index.*
(a) *Transverse diameter of pelves with brim index under 90 and 90 and over.*
In both sexes the under 90 group has a greater diameter.

In 100 males the mean difference = 2.53 ± 1.52 mm. = $1.66 \times$ standard error.

In 66 females the mean difference = 6.075 ± 1.86 mm. = $3.28 \times$ standard error.

Only the female difference is significant.

(b) *Conjugate diameter of pelves with brim index under 90 and 90 and over.*
In both sexes the under 90 group has a smaller diameter.

In 100 males the mean difference = 13.49 ± 1.69 mm. = $7.89 \times$ standard error.

In 66 females the mean difference = 10.57 ± 1.76 mm. = $6.0 \times$ standard error.

In both sexes the difference is highly significant.

It is seen, therefore, that the brim index appears to be a function rather of the conjugate than of the transverse diameter. In the male there is only a small difference between the transverse diameters of the two major groups, but a considerable difference in the two conjugate diameters. In the female, however, the under 90 index group is characterized by a significant difference in both diameters, though the conjugate shows a stronger influence in determining the shape of the brim.

A measure of the growth that occurs in the individual groups can be better determined on the basis of the area of the brim. Brim area will indicate to what extent malnutrition has impaired growth, if malnutrition is associated with low indices.

(c) Planimeter areas of brim in pelves with index under 90 and 90 and over.

In both sexes the mean area for the under 90 group is smaller.

In 151 pelves of both sexes the mean difference=
=3.89±2.43 sq. cm. = 1.6 × standard error.
In 100 males the mean difference =
=6.1±2.64 sq. cm. = 2.3 × standard error.
In 51 females the mean difference =
=2.9±2.87 sq. cm. = standard error.

The indices were higher than platypellic in 43 per cent of the male and in 49 per cent of the female series. In none of the groups shown for area is there a significant difference. Thus a low brim index pelvis may have a large area, and the evidence is not strongly in favour of increased capacity being dependent on higher brim indices. Further information on this point was given earlier. Thus the correlation coefficient for brim area and index gave the following values:

In 100 males $r = +0.256 ± 0.1004$
$= 2.56 ×$ standard error.
In 51 females $r = +0.0798 ± 0.141$
$= 0.566 ×$ standard error.

The association between these two variables is weak, that in the male being possibly significant. A reason for this higher male correlation may be the fact that the lateral boundaries of the brim plane in the male are more streamlined than in the female.

2. Brim area.

The contention that the brim index is merely a function of the conjugate diameter, and the possible inference that the greater the conjugate the greater the brim area, may be met by testing the association between the anterior straight breadth of the sacrum and the brim area. A graph plotted with these variables shows a very close relationship between them, a feature which is more pronounced in the male than the female. There are a few exceptions, and in one direction (narrow sacrum with great area) they tend to be of the anthropoid type pelvis, and in the opposite direction the android type. This explanation, however, did not fit the male exceptions adequately, and a better hypothesis was found—one which accounted for all the exceptions. When the difference between brim transverse diameter and sacral width exceeded the average, the probability that a narrow sacrum would occur with an excessive brim area increased, and vice versa. Hence it follows that the size of the brim plane is determined in a large proportion of cases by the breadth of the sacrum, but even more directly by the brim transverse diameter in which the iliac bulge is, of course, included. Scatter diagrams of the distribution of 101 pelves of which the planimeter area of the brim is known show that area is related most intimately to the transverse diameter, in less degree to sacral width, and least of the three to conjugate diameter.

The sacrum of the giant anthropoids is very much narrower than that of man. Man is the only primate with sacral index above 100, and has developed a sacrum which is wider absolutely and relatively. This comparison with man is striking when taken against the chimpanzee, orang, and gorilla which have all got poorly developed sacral alae: the gibbon has a good alar development and a relatively wider sacrum, and this feature is even more pronounced in certain specimens of Pithecus rhesus. Gorilla has a pelvis with high brim index, great brim area, and narrow sacrum: the area of the brim plane is due to great growth at acetabular and symphyseal epiphyses. The Pecos Indian pelvis shows the reverse features of low brim index, very wide sacrum, and average brim area for small type pelves. The Veddah pelvis lies practically on the regression line of sacral breadth upon brim area.

II. *Development of the sacral alae.*

Pronounced development of the lateral border of the sacral alae has the effect of placing the sacrum relatively further posterior than in the presence of weak development. The result of the former is to increase anterior sacral curvature. Increased curvature would, in a given pelvis, increase antero-posterior brim length. Whether this mechanism actually plays a significant rôle in the brim index variations of a series of pelves may be tested by calculating the correlation coefficients between the curvature index on the one hand and the brim index or the conjugata vera diameter on the other.

r (anterior sacral curvature index and brim index)
$= +0.288 \pm 0.143$ in 50 males
$= 2.014 \times$ standard error.
$= -0.29 \pm 0.125$ in 65 females
$= 1.83 \times$ standard error.

While both values are of a low order, it will be observed that the negative correlation of the female is the expected one: the positive r of the male may have arisen owing to some chance based on brim index factors which have a much greater influence than sacral curvature.

r (curvature index and conjugata vera)
$= -0.09 \pm 0.143$ in 50 males
$= -0.116 \pm 0.124$ in 66 females.

In neither sex is r significant, though here the expected negative value occurs in both.

It is concluded, therefore, that the sacral ala plays a statistically insignificant, and accordingly negligible, part in the adult brim index.

III. *Pathological bending of the girdle due to antero-posterior compression.*

(a) It has already been shown that in the female there is a greater bulge at the iliac portion of the illiopectineal line than in the male. This bulging is obviously a sexual character, but has been confused with hypothetical rachitic bending of bone due to antero-posterior compression.

Fig. 1 shows how closely the brim index follows the conjugate-sacral index. The correlation coefficient for these two variables is $+0.804 \pm 0.1$ in 100 males, and $+0.813 \pm 0.109$ in 61 females. Fig. 2 shows that low brim indices are not associated strongly with great differences between brim and sacral widths. Both these characters are held to be present in rachitic pelves; but it is now seen that one may occur without the other in the absence of gross rickets or, what is more important, in the presence of possible sub-clinical rickets. This is confirmed by the finding, shown earlier, that brim indices of pelves with a marked transverse or iliac bulge are lower, but not significantly lower, than those with a slight bulge.

How do the factors causing this iliac bulge affect true conjugate length and the planimeter area of the brim? The evidence adduced is unexpected, and shows that both the linear and two dimensional values are increased by its development. This suggests that the iliac bulge is dependent on a growth increase which is accompanied by parallel activity in the remaining epiphysial cartilages. On the average, therefore, we are not witnessing mechanical compression followed by pathological warping, but vital morphological variations based on active bone growth. The evidence referred to is as follows.

The pelves were divided into two groups, according to whether the iliac bulge was above the mean or not in the case of the conjugata vera, and below 10 mm. or not for the area. The mean iliac bulge (transverse diameter of brim minus sacral breadth) was 13 mm. in the female and 8 mm. in the male. Conjugate and brim area values were analysed for their respective groups and compared, and it was found

that in all cases the mean values were higher in the groups with greater iliac bulge.

Conjugate vera.

Male mean difference $= 0.79 \pm 2.16$ mm.
                 $= 0.37 \times$ standard error.
Female mean difference $= 4.96 \pm 2.16$ mm.
                 $= 2.3 \times$ standard error.

Planimeter area of brim

Male mean difference $= 7.75 \pm 2.56$ sq. cm.
                 $= 3.03 \times$ standard error.
Female mean difference $= 4.79 \pm 2.72$ sq. cm.
                 $= 1.76 \times$ standard error.

Statistical significance is claimed for the conjugate difference in the female, and the area difference in the male.

It is seen, therefore, that a pronounced iliac bulge occurs in the better developed, and accordingly more robust, pelves. Pathological softening of bone with warping need thus not be postulated to explain an iliac bulge which is above average in 42 per cent of both sexes in the Bantu. Examination of frankly rachitic material will show the degree of bulging that occurs in rickets.

(b) Warping of the brim which is pathological has not been proved to affect the transverse diameter but, if it does occur, it must affect the length of the antero-posterior diameter. The latter diameter will be diminished wherever the bending due to an antero-posterior force is situated. The only possibility that remains, having regard to the argument advanced under III(a), is rachitic bending of the superior rami of the ossa pubis.

The stresses affecting the pubis are not so great as those borne by the body of the ilium, for the pubis is merely a continuation of the lever beyond the femoral fulcrum to give origin to the anterior abdominal wall muscles and some of the adductors of the thigh. Whereas these muscles play some part in the maintenance of the erect posture, the body and adjacent portion of the ala of the ilium form a segment of the pillar that bears the weight of the trunk. The complete collapse of the anterior half of the inlet seen in osteomalacia is a different problem, and may be due to muscular action rather than to mere pressure of the femoral heads on the acetabula: in the erect posture, at least, the lines of force at the acetabula have only a very slight medial tendency.

Because rachitic dry pelves are not available for this investigation, a pronouncement on the pubic response to rickets must be postponed meanwhile. The opinion may be expressed that even in the face of florid rickets, muscular pull based on the functions of the abdominal musculature will be continually exercised even in an incapacitated child; but that in the patient under discussion stimulation of the acetabular epiphyses by the femoral head will be reduced to a minimum. If this suggestion has any basis of fact, it would follow that the Y-shaped epiphysis would be disturbed more than the symphyseal cartilages, with resultant loss of growth in antero-posterior length.

IV. Anterior projection of the sacral promontory.

The female pelvis was examined in conjunction with a series of male pelves with a view to assessing the influence of the forward promontory on the brim index. The apparent anterior projection of the sacrum is based on its proximity to the greatest transverse diameter of the brim: pelves thus characterized may be described as having a short posterior segment of the inlet. These pelves may have both a high index and a great area of the brim; and it does not appear that anterior projection of the promontory is an important factor in producing a low brim index.

What is the cause of the promontory

being situated so close to the greatest brim transverse diameter? In the male it is a characteristic that the posterior extremity of the ilium is rotated downwards so as to cause a narrowing of the greater sciatic notch. While the main effect of this is to carry the lower part of the sacrum forward, the promontory itself is caused to lie relatively further forward than it does in a typically female pelvis. But a more important point seems to be the probability that the position of the transverse diameter has been moved closer to the promontory than the reverse case considered above. This is due to poor development of the iliac bulge mentioned previously. Inspection of a male pelvis will demonstrate a flattened iliopectineal line running from the sacro-iliac joint; this part of the brim may be so slightly curved that measurement shows its widest part to lie at, or close to, the sacro-iliac joint. The typically female pelvis, on the other hand, has a full curve of the ilium tending outwards from the sacro-iliac joint and coming in again on the acetabulum. The greatest transverse diameter in the latter case is accordingly measured near to the centre of the iliac portion of the brim, and thus well anterior to the sacro-iliac joint. The longer the body of the ilium, the longer will the posterior segment be.

The Bantu material illustrates the following facts. (1) The android type pelvis in the female has a comparatively wide sacrum. It may be presumed that considerably increased growth at the symphysis pubis would be required to provide sufficient bone for a good bulge in the iliac region. (2) The anthropoid type pelvis has the narrowest sacrum, with the gynecoid type intermediate between android and anthropoid in this respect. (3) The ratio of the lengths contributed by pubis and ilium to the formation of the brim are not different in high and low index brims.

The general conclusion follows that loss in the antero-posterior length of pelves which appear to have an anterior projection of the sacral promontory is compensated by narrowness of the brim. The tendency for such pelves is to preserve a brim index comparable in value with the mean. Low values are likely to occur when sacral breadth is pronounced, a possibility illustrated well by the Pecos material.

DISCUSSION.

I. *Radiology and the position in general.*

No student of pelvic morphology can fail to be impressed by the implications of the pelvic brim index. In the study of the Bantu pelvis, and more particularly of its ontogenetic development, the index has played a prominent rôle; and for more than a year one's chief considerations have been guided by the belief that the dolichopellic pelvis occurs more frequently in privileged communities than in those stricken with malnutrition and morbidity. The view is widely held that in certain races the dolichopellic pelvis predominates. This type of pelvis is the most efficient in parturition and is comparatively rarely associated with dystocia. Quite unprecedented momentum was given to the nutritional aspect of pelvic form when Greulich and Thoms (1939) reported that in a series of 104 nulliparous nurses of superior economic and physical status the brim index was considerably higher than in large series of Thoms' free hospital patients. Not only was the index higher in the nurses but, what is more significant, these young American women gave an average value of nearly 100. No discovery in the field of pelvic development and anatomy was more important than this finding which has been commented upon by others, e.g. Ince and Young (1940) and Nicholson (1945).

The Bantu studies have led to a pronouncement concerning the evolution of the

pelvis (Heyns, 1946). This and other considerations have consistently proved to be irreconcilable with the view that highly favourable living conditions have a pronounced influence on the development of the capacious, ultra-dolichopellic pelvis. In revising this view the surprising fact emerged that the only authentic evidence in its favour was that produced by Thoms; and it appeared probable that this evidence had been more impressive because of its advent at a time when much thought was being given to nutritional problems. It is curious that Thoms did not make greater endeavour to emphasize his discovery. However, his results were questioned in spite of the belief that human physical development in the United States has far outpaced that in other contemporary countries, and that a comparable peak of growth has probably been reached by none save the ancient Egyptians and Greeks (Hrdlicka: Mills, 1937).

It has been questioned (Heyns, 1944) whether Thoms' radiographic method of pelvimetry was above criticism, but our familiarity with the possibilities of his technique reassured us; and there remained the almost unassailable point that an error present for one series would apply correspondingly to another. Furthermore, as the hospital patient series provided a mean index similar to that of English women and the Bantu, it appeared that Thoms' nurses must in fact predominantly possess such pelves as occur in not more than 20 per cent of other known groups. An investigation into the matter has provided evidence which shows that Thoms' clinic women probably have a mean brim index well below 90, and that his nurses have indices not at all different from those of English or Bantu women. The proof of this assertion has been published elsewhere in order to abbreviate the argument of the present report (Heyns).

II. *Outline of the effects of epiphysial growth.*

A glance at Table I will show that growth activity diminishes steadily with the advance of ontogenetic age. This is true for all the calculations shown, without exception, and these include increase in volume and in length of the bone of the girdle proper. While it is true that the first three years of life represent a very active growth period, the foetal period exhibits greater activity which can be shown to decline appreciably during each trimester. It is, therefore, more precise to visualize the increase of bone as becoming *slower and slower; and to seek linear increase over arbitrary periods only in an* attempt to study the relative activity of different epiphyses during those periods. It will be realized that conclusions drawn from growth data are restricted by the fact that all the cells present at a given time are not proliferating: growth in length (not girth) occurs only at epiphysial ends of the existing length of bone, and the rest of the bone may for our particular purpose be considered as passive and stationary. The calculations in Table I are based on the proportion of increase to previous value, and carry the presumption that the greater the segment of bone the greater are its advantages for growth. The surface of an epiphysis is no doubt greater at 8 years than at 2 years of age, but it is obvious that epiphysial growth cannot be expected to be proportional to diaphyseal length.

Should linear variables in the brim plane be considered, it will be found that anterior sacral breadth and the brim transverse diameter increase relatively by about the same length during the three postnatal periods of birth up to 2 to 3 years, 2 to 8 years, and 8 to 14 years. The conjugata vera, on the other hand, grows during these phases respectively 17 mm., 29 mm. (or possibly more), and 23 mm. From puberty

to the adult state the conjugate increase is 5.6 mm. in the female (male 1.3 mm.), brim transverse increase 19.6 mm. in the female (male 12.6 mm.), and sacral breadth increase 14 mm. in the female (male 11 mm.).

Table II is an attempt to estimate the exact amount of linear growth at the three

physeal growth has been based on the difference between the transverse diameter of the brim and the breadth of the sacrum, for it follows from the premise stated that the iliac bulge can occur only as the result of growth at the symphyseal epiphyses.

If the above argument is accepted, Table II shows that growth at the symphysis is

TABLE II   PELVIC GIRDLE

Growth During Ontogeny at the Three Double Sets of Epiphyses.

The figures indicate the growth in mm. that has taken place between two consecutive periods.

| Period | | | Site of Epiphysis | | |
			Symphysis	Sacrum	Acetabulum
I(a)	The last prenatal 6 months		2.25	25.1	25.25
I(b)	The entire prenatal period		?	37.0	33.0
II	Infancy (2 to 3 years)		6.0	14.0	17.0
III	At 8 years		6.0	17.0	29.0
IV	At 14 years (early puberty)		3.0	17.0	23.0
V	After puberty Female		5.6	14.0	5.6
	Male		1.6	11.0	1.3
			T.B.—sacral width	Sacral width	Conjugate vera
Adult means	Male		20.6	98.8	107.6
	Female		16.8	95.0	103.3

sets of epiphyses that enter into the present problem. The assumptions involved here are that increase in antero-posterior length can only occur at the acetabular epiphyses, and increase in lateral or transverse length at both sacral and symphyseal epiphyses. The possibility that muscular traction at the symphysis pubis in a posterior direction may cause physiological bending with decreased curvature or flattening of the brim has for the present been disregarded. In Table II the figures in the column headed " Acetabulum " are based directly on increase in conjugata vera length, those under " Sacrum " being similarly derived from the breadth of the sacrum where it is in relation to the iliopectineal line. Sym-

comparatively slight, and that this growth is at its lowest level from about 8 years to puberty. During this phase the acetabular epiphyses are making a considerable contribution to conjugate length, an activity which is most pronounced between 2 and 8 years. This would explain the preponderance of conjugate over transverse diameter which has been observed by other investigators, and is the reason for the prevalence of dolichopellic pelves at this time. From puberty to the end of ontogeny epiphysial growth at the symphysis reaches such a high level that it progresses pari passu with acetabular increase in length. A new feature manifests itself at this time, for the sex factor has emerged and is

associated with much diminished, though equal, growth at these epiphyses in the male. The fact that the adult male pelvic brim exhibits a very poor iliac bulge strongly supports the view that this difference between brim and sacral widths is due to bone growth at the symphysis rather than to bending of the bone by antero-posterior muscular force. By the same token, it is improbable that the iliac bulge is produced by the counteraction of a bending moment due to augmented osseous proliferation on the outer aspect of the body of the ilium.

It cannot be denied that during the cartilaginous prenatal stages bending of the pubes may require to be postulated in order to account for the rounded contour of the forepelvis, for it has not been proved that symphyseal growth occurs in the first trimester. About the fourth intra-uterine month sacral breadth is 2.25 mm. greater than the greatest brim transverse diameter. This may mean that sacral growth has been much more rapid than pubic growth at the symphysis, or alternatively that pubic growth has been negligible and the rounded shape of the forepelvis is due to mechanical curvature based on muscular forces. At the end of foetal life, however, the brim transverse is only 0.1 mm. less than sacral breadth, which suggests that in later foetal life symphyseal growth has taken place. The first few years of postnatal life are characterized by pronounced growth at the symphysis (Table II). It must be recognized that the bending of bone referred to would take effect in the pubic region, and that this hypothesis is not called for except to explain the form of the forepelvis in the possible absence of symphyseal bone growth in early foetal life. All the available evidence points to symphyseal growth as the basis of the iliac bulge.

Sacral growth during ontogeny is reflected in Table II, and it is seen that adolescent growth is similar in the two sexes. During adolescence the lateral and anterior epiphyses grow at an equal rate in either sex. Two female features are (a) that growth exceeds that of the male, and (b) that the symphyseal epiphysis exhibits pronounced rejuvenation. The factors responsible may be hereditary or sexual, or both. If sexual, increased vascularity and hormones are possible causes. It is improbable that during puberty vascularity is different in the sexes, but it is possible that the genitalia afford an increased circulation to the anterior pubic region rather than to the lateral and posterior parts. With reference to endocrine influences, the evidence is conflicting. On the one hand hypo-ovarianism is associated with late union of epiphyses and excessive growth in stature; on the other, it is known that callus formation (Hills and Weinberg, 1941) and ossification (Pfeiffer and Gardner, 1938) are stimulated in the presence of oestrogens. The latter processes are not directly related to epiphysial growth; and it is well known that thyroid, parathyroid, and hypophyseal secretions are all intimately concerned with growth in general. The problem of pubertal bone growth is, therefore, a complex one.

What is known from observation, however, is that the limb of the Y-shaped epiphysis between pubis and ilium is the first acetabular unit to unite by osseous fusion, an event occurring in late puberty; but that the symphyseal epiphysis becomes obliterated towards the end of ontogeny. Throughout ontogenetic development the evolution of the erect posture is associated with increased muscular strain at the symphysis pubis, and it is possible that these strains result in stimulation of growth at the symphysis. As the mammalian scale is ascended, the pelvic brim develops from a triangular-shaped girdle to one with an ovoid and

finally a rounded contour. It was submitted elsewhere (Heyns, 1946) that the purpose of evolution is to produce in man the ultra-dolichopellic pelvis. This hypothesis was discussed as being compatible with Bolk's retardation and foetalization concept (1925–26) which suggests that morphologically the apes have advanced much further than man along the road of evolution. These views are merely hypothetical, and the present report explains the mechanism by which the end-result is obtained, and how the dolichopellic pelvis of childhood becomes the platypellic pelvis of the adolescent and adult. The present report is stated to be preliminary for two reasons: (1) While general observation suggests that the greatest proliferation and accumulation of bone on the outer aspect of the body of the ilium is not associated with conspicuous iliac bulge, this correlation has not been studied exhaustively. (2) Cartilaginous activity at the symphyseal epiphyses is being studied histologically both in the foetus and in the child, and collection of the post-natal material is slow.

III. *Physiological bending of the pelvic girdle.*

It has been argued that rickets in mild form cannot on the evidence available be convicted of flattening the pelvic girdle. There can be little doubt, however, that physiological bending of the bone must occur during ontogenetic development. The only reasonable explanation, for example, that accounts for the phenomenon of the iliac bulge is that symphyseal epiphyses contribute to the perimeter of the girdle to the accompaniment of bending. This bending will occur in front most directly, and produce a rounded contour of the forepelvis; but bending forces can also be transmitted to the ilium further back. It is certain that increase in sacral breadth cannot contribute to the iliac

bulge. Thus it is necessary to formulate a working hypothesis which will explain physiological bending. The adoption of the erect posture is responsible for the play of many forces in the region of the body of the pubis, for the anterior abdominal muscles and the adductors of the thigh gain origin here, and the psoas muscles make pressure on the superior pubic ramus. These forces probably pull the symphysis backwards and contribute to the rounded contour of the forepelvis (compare other primates and lower mammals). The conjugate shortening that follows is restored by growth at the acetabular epiphyses. Epiphyseal growth at the symphysis may, therefore, be devoted largely to widening of the brim in the region of the ilium, such bending as occurs at the pubes having been produced mainly by muscular forces. It is true that more symphyseal growth may occur than is shown merely by increase in the iliac bulge, but it is possible that the latter may represent a great preponderance of the growth.

The bending moments set up at the iliac bulge by increase in sacral breadth may be counteracted by periosteal growth which is greater on the outer than on the inner aspect. This will have the effect of increasing the bulge. Examination of pelves, best exemplified by the male, shows that the thickest bone growth in this region usually corresponds to the smallest bulges. To enter further into this problem of bending of the girdle would lead to pure conjecture and an attempt to explain such hitherto unsolved mechanical aspects of bone growth as remodelling.

A few applications of the above hypothesis may now be considered. The iliac bulge increases with time up to adolescence and, therefore, as the bone becomes more rigid. It appears unlikely that bending due simply to bone softening would behave in this chronological manner. It seems as if

perfectly balanced growth in the human pelvis is characterized by active growth in sacral width, and an unexpected increase at the pubic symphysis—both factors tending towards great width of the brim. And this tendency is essentially a human feature, only poorly exhibited by the other primates, but most conspicuous in the human female. Activity at the Y-shaped epiphysis in this nicely balanced pelvis is, however, so pronounced that a mesatipellic instead of a low platypellic brim index is produced at the end of ontogeny. It is obvious that sometimes the symphyseal epiphysis will outgrow the acetabular and produce platypelly, and sometimes the reverse process will lead to dolichopelly. In the background of all this activity there hovers the sacrum: it has a profound effect on the ultimate index of the brim. There is no evidence at present to support the view that superb nutrition will permit of less bending and result in a higher incidence of ultra-dolichopellic (anthropoid) pelves. In truth, the facts are opposed to such a possibility. Inspection of round and even low index pelves gives the impression of unrestricted growth: they are usually capacious and have a marked iliac bulge which suggests active increase of osseous tissue.

Practically all pelves with brim index below 80 have either unusual relative sacral breadth or a marked iliac bulge, or both. Where indices of 100 or over occur, the reverse is the rule, viz., relatively narrow sacrum with slight iliac bulge, or both. The factor on which the " relative " size of the pelvis may be usefully based in this connexion is the conjugata vera length. Thus pelvis A730, 721 with conjugate 99 mm. might be expected to have dimensions below the average: its sacral breadth of 105 mm. is near the average but broad for such a small pelvis; the iliac bulge contributing 30 mm. is conspicuous—and the brim index finally shows the low figure of

73.33. This pelvis has a brim area above the average, and it is submitted that inlet size was increased by relatively great growth at the sacral and symphyseal epiphyses. It is obviously possible that retardation of acetabular growth was the primary feature in the development of this pelvis, and that in fact the inlet should have grown excessively. The contention is, however, that robust growth at the anterior and posterior epiphyses gave the pelvis adequate capacity, and that it was not primarily warping that reduced conjugate axis and index and thus diminished the inlet area.

A682,683 had a brim index of 69.63 with conjugate diameter only 94 mm., sacral breadth 114 mm., and iliac bulge 21 mm. The brim area was just less than the average. A831,844, an ultradolichopellic pelvis, had a brim index of 103.65. The conjugate diameter was above average at 115 mm., but sacral breadth below average at 101 mm. As the iliac bulge contributed only 10 mm., the greatest transverse diameter was 8.5 mm. below average and the brim index rose to over 100. A831 with index 103.65 and A682 with index 69.53 have equal brim areas. The three specimens referred to are female.

Increase in sacral breadth alone augments the transverse axis of the brim by a proportional factor and the conjugate axis by about half this factor. This may be shown experimentally by expansion in metal rings made to represent the girdle. The iliac bulge is not affected.

SUMMARY.

PART I. GENERAL.

A. The significance of the pelvic brim index is stated, and reference made to the belief that under favourable, healthy living conditions the index appears to be higher than in circumstances of poverty.

B. The brim index in different races is surveyed, and Bantu figures are included.

C. Ontogeny and phylogeny are considered under two heads: (*a*) General, and (*b*) Bantu data.

PART II.

ANALYSIS OF ANATOMICAL OBSERVATIONS.

A. The validity of certain current hypotheses is tested: correlation coefficients for brim index and brim area, and for brim index of conjugata vera over sacral breadth; the basis of antero-posterior flattening in rickets; the relation of bulging at the iliac portion of the illiopectineal line to rickets.

B. The factors influencing the brim index are considered under four heads.

1(*a*) Epiphyseal bone growth.

The mechanism of increase in size of the pelvic girdle is considered; and the increase during ontogeny of the brim axes and sacral breadth is analysed. The effect of rickets on growth processes is discussed.

1(*b*) A statistical analysis of individual variables and their relation to the brim index is presented.

2. The effect of good development of the sacral alae. This was found statistically to be negligible.

3. Pathological bending of the girdle due to antero-posterior compression is considered, but there appears to be no evidence in favour of this possibility in cases of mild rickets.

4. The effect on the index of anterior projection of the sacral promontory is analysed anatomically, and an explanation offered of its lack of significance relative to index variations.

DISCUSSION.

1. Radiological implications and the position in general. There is no evidence that malnutrition of moderate degree influences the brim index.

2. An outline of the effects of epiphysial growth is given. Emphasis is laid on bone growth at the symphyseal epiphysial cartilages which are an important factor in increasing the transverse axis of the brim. It is submitted that it is to activity in this region that the human girdle owes its morphology.

3. Physiological, as opposed to pathological, bending of the pelvic girdle is considered to be present. The mechanics of this factor is complicated, and is not susceptible of simple experimental proof.

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The Technique of the Lower Segment Caesarean Section

BY

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ALTHOUGH the advantages of the lower uterine segment operation have long been recognized, many obstetricians, even nowadays, prefer the classical Caesarean section, due probably to the difficulty of access to the lower uterine segment region.

When, however, the technique of this excellent operation has been more fully developed, the difficulties in performing it will be overcome and this will lead to even better results than are now obtained.

In view of this there is a great need for exchange of ideas among obstetricians about the technique used by them in performing the lower segment operation. The fact that modern obstetrics permits a great number of relative indications for Caesarean section makes the matter still more important.

The technique of Caesarean section used in the Paderewski Hospital allows us, in our opinion, to overcome many difficulties caused by insufficient access to the operation field. At the same time some factors can be avoided, which, apart from making the operation more difficult, may prevent a quick convalescence and the attainment of the best anatomical and functional results.

It has long been our custom to perform the operation in the middle of the first stage of labour if conditions permit. As labour becomes more advanced a still lower part of the uterine segment can be chosen for transverse incision. When the cervix admits the insertion of 4 fingers, the incision can be made in the supravaginal part of the cervix, just above the attachment to the vaginal wall. The passive uterine segment is greatly expanded at this time and the scar after complete involution of the uterus is very small for this reason. The risk of rupture of the scar is thus considerably diminished in the event of a subsequent labour. However, there is no objection to performing the lower segment operation even before the onset of labour, because, as we know, the lower uterine segment becomes sufficiently thinned during the last weeks of pregnancy. In cases, however, where the lower uterine segment is not sufficiently expanded, it may be advisable to make a longitudinal incision in the uterine wall instead of the transverse one, the technique of which is here described.

The patient is placed in the usual position for any gynaecological abdominal operation. Trough-shaped knee supports are used in place of the lower leaf of the operating table, and the legs are drawn apart as the patient lies on it. This leaves sufficient space to enable a second assistant to stand between the legs during the operation, giving him good access without interfering with either the surgeon or the first assistant. The thighs are slightly raised above the level of the trunk. The operation is performed in the Trendelenburg position, the degree of inclination depends upon the state of the patient and is such as just to make the lower abdominal wall horizontal. Pfannenstiel's transverse abdominal in-

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cision is generally used in our hospital. Besides giving good cosmetic results, it probably diminishes the symptoms of peritoneal reaction after the operation. Although this opening is usually sufficient for the lower segment operation, it takes longer to make, and the access to the operating field is less than with the longitudinal incision. For these reasons it is best to employ the usual longitudinal opening of the abdomen in urgent cases and for obese patients.

If the abdominal incision in the middle line is used it is of great importance to *incise the abdominal fascia and the tendons* between the pyramidal muscles as far as the symphysis pubis. This facilitates access to the lower uterine segment. The bladder runs little danger of being cut by this incision. The danger of injury to the bladder must be taken into account only when incision of the peritoneum and its preperitoneal fat is made. For this reason the first incision of the peritoneum should be made high, and afterwards extended downwards with care.

After the opening of the abdominal cavity two abdominal retractors may be introduced which are directed downwards and laterally. This gives better access to the lower uterine segment than the use of only one broad retractor. In order to prevent the liquor amnii getting into the peritoneal cavity two large swabs wrung out in physiological saline are put between the abdominal wall and the uterus. The swabs converge behind the upper part of the abdominal opening and their lower ends lie in both the lateral parts of the uterovesical fold of the peritoneum. This isolates the peritoneal cavity sufficiently from the immediate operation region.

From this point the operation can be divided into the following stages:

(1) *Detachment of the bladder.* The uterovesical fold of the peritoneum is incised transversely from one round ligament to the other. The loose connective tissue under the peritoneum which surrounds the bladder is dissected up to the uterine wall and later the bladder is detached by blunt dissection to the region of the vagina.

Details. The peritoneum covering the bladder is held in the centre by surgical tissue forceps about an inch below the place where it is attached to the uterine wall. The incision into the stretched peritoneum is made by blunt-pointed scissors half an inch below the tissue forceps and it is extended horizontally on both sides as far as the round ligaments. If the peritoneum is folded, the cutting can be made easier by the assistants raising and holding the round ligaments in position to stretch the peritoneum.

Holding up the peritoneum of the bladder in the centre with the dissecting forceps, the loose connective tissue under it and around the bladder is stretched and clearly visible. By cutting this tissue with scissors, held concave side to the uterus, the right layer between the uterus and the bladder is reached. Later by blunt dissection with closed scissors, still held in the same way, the bladder is detached from the uterine segment, first in the middle line, then laterally. Great care must be taken not to go beyond the uterus towards the sides in order not to injure the blood vessels in the parametrium, and not to enlarge the wound space unduly. If the correct layer of dissection has been chosen there should be no bleeding during the exposure of the lower segment. This blunt dissection can also be performed with a straight retractor* instead of scissors, because the connective tissue is usually sufficiently loose. A thin layer of connective tissue is left on the surface of the lower segment.

On very rare occasions the exposure of the lower uterine segment must be made by cutting with scissors between the walls of the bladder and the the uterus when post-operative or post-inflammatory induration of the connective tissue exists. For this purpose the bladder wall is held up by the tissue forceps directly above the place of dissec-

*A narrow, oblong, slightly hollow blade with a bayonet-shaped link between blade and handle.

Text labels within the figure:

THE LONGITUDINAL FOLD OF THE LOWER SEGMENT INCISED BETWEEN THE TWO FORCEPS.

THE UTERO-VESICAL FOLD OF PERITONEUM INCISED TRANSVERSELY.

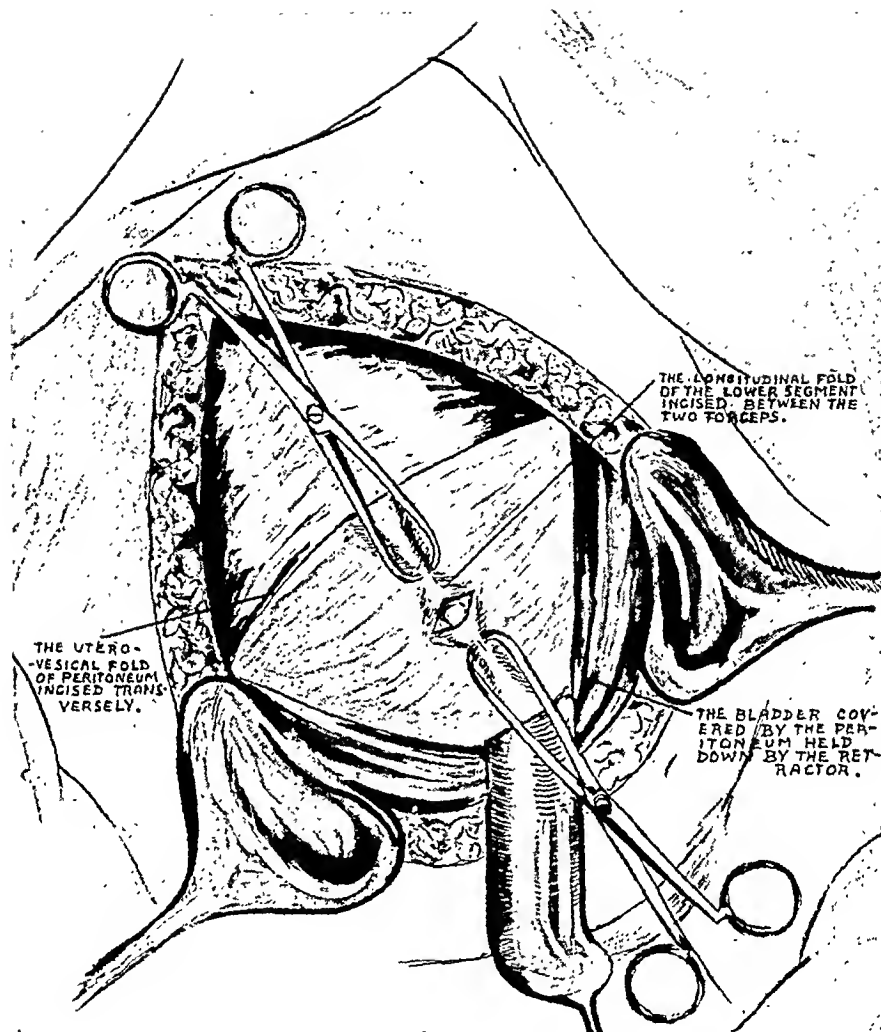THE BLADDER COVERED BY THE PERITONEUM HELD DOWN BY THE RETRACTOR.

FIG. I.

The abdominal cavity is opened along the middle line. The detached bladder is held down by a retractor. The exposed lower uterine segment is folded by two forceps and a small incision is made between them.

[Drawn by Z. Szulec, Polish School of Medicine, Edinburgh.]

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tion. Such cases are very rare and, if met with, the area involved is small.

(2) *Transverse incision of the lower uterine segment*. A longitudinal fold of the wall of the lower segment is made by clamping it with two Allis's forceps one above the other. This fold between the two forceps is cut through to a sufficient width to permit the tube of the aspirator* passing through it in order to drain off the liquor amnii (Fig. 1). After this liquid is withdrawn the incision is enlarged transversely right and left about 2½ inches on each side.

Details. By clamping the exposed uterine wall with two Allis's forceps one above the other we form a longitudinal fold. Holding the forceps vertically (the surgeon the lower one, the assistant the higher one) the surgeon makes a transverse incision half an inch long with a knife between the forceps. The raising of the fold of the uterine wall prevents all danger to the child. In any case in which the lower uterine segment is not thin enough to permit the clamping of Allis's forceps through its whole thickness, the forceps must be transferred—perhaps more than once—from the more superficial to the deeper layers.

The edges of the uterine segment do not bleed because of the compression made by the above-mentioned forceps. The cannula of the aspirator is inserted in the opening and pushed gently upwards between the presenting part of the child and the uterine wall into the amniotic cavity and the liquid is almost entirely drawn off. The incision is enlarged by cutting with straight scissors to the right and to the left, slightly curving upwards if the previous incision has been placed very low. During this enlargement the uterine wall is pulled up to avoid injury to the child. An incision about 5 inches long is sufficient for the extraction of the foetus. The edges of the uterine incision bleed very little, if the lower uterine segment is well stretched and expanded as a result of labour. Otherwise, there may be free bleeding usually near both

angles of the wound but it is easily checked by clamping the edges with Allis's forceps while cutting. The incision is placed ¾ inch below the upper edge of the peritoneum, leaving sufficient room for sutures. If the lower uterine segment is widely expanded the incision can be made even lower, but not too low because of the pubes, and in order not to increase the difficulties of access to the operation field.

(3) *Extracting the child*. In the case of a vertex presentation the obstetric forceps are applied for the extraction of the head. Then the surgeon, pulling with the index finger placed under the axilla, disengages the anterior shoulder and arm and then the other shoulder and arm in the same way.

In the case of a breech presentation the surgeon first seeks and disengages both legs, then the shoulders and arms, and extracts the head by means of a manoeuvre very similar to the Mauriceau-Smellie method.

Details. If the incision in the abdomen is rather small the abdominal retractors are withdrawn in order to have more room for extracting the child. The forceps in the middle of the lower edge of the incision is also removed. The midwifery forceps is applied under the guidance of the hands. If the head is partly or wholly engaged the forceps is applied with the pelvic concavity turned to the pubes. If the head is movable above the brim the pelvic concavity is turned the opposite way. The extraction of the head is completed by directing the traction forwards and upwards, so that the vertex appears in the opening first after which the forehead is gradually eased out behind it. For a high head, one blade of a pair of forceps may be used. It is introduced from the pubes and then passed gently behind the head. The head is drawn out through the opening by raising the blade of the forceps and pushing the head with the other hand in the direction of it. The extraction of the body is completed by pulling with the finger passed under the anterior axilla, so that the shoulder is withdrawn and the arm disengaged, then the other shoulder and arm in the same way. After the child has been separated and handed to the nurse, the abdominal retractors are applied again.

*The cannula of the aspirator should be 10 inches long, curved and provided with several small openings around its end.

4) *Removing the placenta.* An injection of 1 c.cm. of pituitrin is made into the active part of the uterine wall. The placenta is removed by firmly pressing on the uterine fundus and pulling the cord gently, but not before the uterus is very well contracted as a result of the pituitrin injection.

Details. Immediately after the child has been extracted the assistants swab away the rest of the liquor amnii and the blood from the operating field and clamp the bleeding vessels. After the surgeon has handed the child to the nurse he injects into the active part of the uterus 1 c.cm. of pituitrin. In order to do this he exposes the anterior wall of the uterus by pulling down the upper edge of the incision with Allis's forceps. While waiting for the injection to act two Allis's forceps are placed at the right and left angles of the incision. The number of Allis's forceps used depends on whether the wound is bleeding or not. If the wound is not bleeding 4 forceps, at least, are used; one at each end and one each at the upper and lower edges of the incision. This gives the operator better control of the uterine cavity and also helps him later in the insertion of sutures.

When the uterus is well contracted the placenta is separated and removed by pressure on the fundus of the uterus and by gently pulling the cord. The pressure should not be too great, lest the placenta be torn. It is seldom necessary to separate and remove the placenta by hand as the above method is quite sufficient in most cases. When the surgeon is sure that the whole of the placenta and membranes are removed, the cavity of the uterus is packed with a swab. It stimulates the contractions of the uterus and prevents bleeding from the placental site during the first stages of suturing of the uterine incision. The packing is removed when two-thirds of the uterine incision is sutured.

(5) *Suturing the uterine incision.* The opening of the uterus is closed by two tiers of continuous catgut sutures.

Details. A continuous catgut suture is inserted beginning from the angle on the assistant's side. The assistants raise and join the two edges of the

incision by holding them together with forceps. The stitches are inserted 3 to 10 mm. from the edge of the wound according to the degree of expansion of the lower uterine segment. If the wall is greatly thinned the distance from the edges must be nearer 10 mm. The sutures should just miss the decidua. Almost every third stitch is looped. The next tier of continuous catgut suture covers the first one and folds the wall of the lower uterine segment. This second suture may also be interrupted. The stitches of this tier must not be too wide nor too deep in order to avoid injuring the blood vessels especially near the two angles of the wound where the risk is greater because of the larger vessels. Last of all the incision in the utero-vesical fold of the peritoneum is closed with a continuous catgut suture.

(6) *Toilet of the peritoneal cavity.* After the swabs are withdrawn the lower part of the peritoneal cavity, especially the pouch of Douglas, should be wiped out with gauze. In cases where infection of any kind is suspected the peritoneum of the vesico-uterine pouch and pouch of Douglas is dusted with sterile sulphanilamide powder, as also the tissue between the layers during the closing of the uterine incision.

Then the abdominal wall is closed in the ordinary way.

DISCUSSION.

In the above description of the technique used some facts of particular importance should be emphasized. They concern first the detachment of the bladder. The incision of the vesico-uterine fold of the peritoneum should not be too close to the peritoneum where is it firmly attached to the uterine wall. This makes it much more difficult to find the right layer between the bladder and uterine wall and often causes the cutting of blood vessels. Later this hinders the operation. If the incision in the peritoneum is performed about $\frac{1}{2}$ to $\frac{3}{4}$ of an inch away from the firmly attached peritoneum then it exposes the very *loose*

connective tissue which does not contain large blood vessels. The latter extends between the dissecting forceps, which draws up the bladder and the uterine wall and is cut half way with scissors in the direction of the uterus. This leads to the right layer and later permits of the bladder being detached from the lower segment by blunt dissection.

The bloodless exposure of the lower segment prevents the formation of small hematomata in the connective tissue, gives a clear field for the operation and contributes to clean healing.

The next important point to be considered is the making of a longitudinal fold in the lower segment wall. This fold is held in position by clamping it with two Allis's forceps and making a small incision between them. The blood is thus prevented from flooding the incised surface and the liquor amnii is drawn off through this small opening and is almost entirely prevented from entering the peritoneal cavity. This is of importance if the liquor amnii is infected.

The conditions assured by this method facilitate the extension of the incision in the lower uterine segment. If, however, some bleeding should occur, it can easily be checked by clamping with Allis's forceps.

Finally it is of great importance to wait until the injection of pituitrin given into the active part of the uterus has contracted the uterine muscles well before removing the placenta. If the contraction is strong, pressure on the fundus of the uterus and slight pulling on the cord will completely separate the placenta and its extraction as well as that of the membranes becomes an easy matter. Manual removal or exploration of the cavity is thus avoided in most cases.

Furthermore, only slight bleeding, if any, occurs as the result of good contraction of the uterus due to the action of pituitrin injected into the active part of the uterine muscle in proper time.

Fibroids in Pregnancy

(An Analysis of 122 Cases Treated in University College Hospital, London, from 1934 to 1945.)

BY

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INCIDENCE.

SPENCER[1] said that fibroids occur about once in every 150 pregnancies, and this figure seems to be a fair average. Mussey and Hardwick[2] gave an incidence as high as 1.9 per cent and F. J. Browne[3] one as low as 0.28 per cent. However, it is hard to give an accurate estimate, for, although some intramural fibroids become superficial and thus more easily palpable as pregnancy advances, others become flattened and softer and progressively more difficult to feel. Pierson[4] noted 250 cases in 30,836 pregnancies (0.8 per cent), but regarded only 191 of them as of "clinical significance," whilst Mussey and Hardwick[2] thought .that only 97 of their 297 cases were important. There is thus a wide variation of individual opinion in interpreting "clinical importance," and therefore the term is of little value.

In University College Hospital over the past 12 years the following incidence has been noted:

Number of pregnancies		...		15313
Number of cases with fibroids:				
Primigravidae	...	...		81
Multigravidae	...	...		41
Total	...	...	...	122
Incidence ...	...	...	...	0.79 per cent

Watson's[5] contention that parous women are less liable to develop fibroids is widely accepted, but no definite deductions can be made from these figures as more primigravidae than multigravidae have been treated in the hospital.

Age Incidence. The present series of cases show that this complication is found relatively frequently in elderly primigravidae. Spencer[6] said that he usually found one or more fibroids in primigravidae of 35 years and upwards, but this high incidence must be exceptional. Many of the patients here had been married for a number of years, a fact which suggests low fertility. Indeed, Graves[7] and Beckwith Whitehouse[8] both estimate that 30 per cent of women with fibroids are sterile.

Total cases	...	...	...	122
Number of primigravidae of 36 years of age or more	...	...	...	25 (20.5%)
Average age of *all* cases	...	...	34.3 years

The youngest patient was 25 and the eldest 46 years old.

EFFECT OF FIBROIDS ON PREGNANCY.

In this series of 122 cases, only 49 (40 per cent) had normal pregnancies, and this figure does not include toxaemia, the incidence of which was not increased, and malpresentations which were more common. Thirty-eight of the normal cases were primigravidae, and 11 were multigravidae.

Premature interruption of pregnancy.

It may be of interest to note that 15 out of 102 cases where records are available (14.7 per cent)—6 primigravidae and 9 multigravidae—gave a history of at least 1 miscarriage. In Watson's[5] series of 157 cases it occurred in 45 per cent, whilst Spencer[9] maintained that only submucous fibroids caused abortion, and these incidentally especially predispose to sterility.

Threatened abortion. (Where pregnancy continued).

Eleven cases were admitted, and 1 readmitted to hospital with a threatened abortion (9.8 per cent). The bleeding took place at any time from very early pregnancy up to the 25th week, and in 9 patients it occurred after the 12th week.

Abortion (where pregnancy terminated before the end of the 28th week).

Seventeen patients miscarried (14 per cent), 10 of them after the 3rd month. Polak[10] found that 21 per cent of his patients aborted, and Pierson[4] 8 per cent.

In consideration of all the facts relative to the incidence of abortion it would be unwise to form any conclusions from these figures. One fact should be noted—the greatest proportion took place after the 12th week, a point emphasized by Pierson.[4]

Premature labour. This took place on 10 occasions (twice in a twin pregnancy), and 6 of the 12 infants were lost.

Of the 122 cases under consideration abortion took place in 17 patients and premature labour was noted in 10. Thus, premature interruption of pregnancy took place in 22.1 per cent of cases and the foetal mortality in them was 79.3 per cent. Pierson[4] gives a very similar figure—premature interruption of pregnancy took place in 39 cases (24.1 per cent) and the foetal mortality was 78.7 per cent.

Pressure symptoms. No attempt has been made to assess the relative importance of the fibroids in the causation of these symptoms. Only 1 patient had retention of urine. She was suffering from epilepsy which was increasing in severity, and a total hysterectomy was performed in the 3rd month after the urinary symptoms had been alleviated.

Impaction,[11] torsion of a pedicle,[12] infection, intraperitoneal bleeding from a ruptured vein,[13] ectopic pregnancy[14] and placenta praevia were not encountered.

EFFECT OF PREGNANCY ON FIBROID.

Size. Fibroids become larger and softer as pregnancy advances owing to oedema, increased vascularity and hyperplasia and hypertrophy of the muscle fibres.

Displacement. The growing uterus tends to pull the fibroids upwards out of the pelvis, and, in the last 3 months of pregnancy, those sunk deep in the muscle may be more easily palpable as the uterine wall is thinned out. During labour, fibroids which at first sight appear to offer insuperable obstruction, may be drawn over the presenting part. No case was noted where this occurred, for when a fibroid was situated below the presenting part and appeared as if it might obstruct labour Caesarean section was carried out.

Red degeneration. Watson[5] regarded this as the most frequent complication, and the present series where it occurred in 22 patients (18 per cent), 19 of whom were admitted to hospital, confirms his view. It was met with at any time from the commencement of gestation until term—in fact one woman who was never ill enough to require hospitalization complained of local pain and tenderness throughout her pregnancy, and another had severe pain from this complication during labour and the first few days of the puerperium.

All cases, except 2, were treated conservatively. Laparotomies were performed on 4 occasions when the diagnosis was in doubt and the patient in great pain. In the 2 patients under consideration a myomectomy was done at the 12th and 18th week respectively, without disturbing the pregnancy. One was not delivered by the hospital and her subsequent history is unknown. The other had a forceps delivery of a healthy child at term. In the case of the other 2 patients, operative treatment was not undertaken.

Two explanations have been given for the more frequent incidence of red degeneration during pregnancy. Browne[3] suggests that the increased fibrinogen content of the blood in pregnancy favours thrombosis in the arteries supplying the fibroid with a consequent infarction, and Charlewood[15] that the increased growth of the fibroid under hormonic influence outstrips the blood supply, which may be further diminished by the tumour becoming exteriorized.

ANTEPARTUM HAEMORRHAGE.

There were 5 cases of antepartum haemorrhage for which a cause could not be found (4.1 per cent). Bleeding took place between the 32nd and 38th week and in no case did it occur more than once. Two patients went into labour normally at term, Caesarean section was performed twice at the 35th and 38th week respectively, and the fifth patient had a breech delivery. The last child was lost.

From 1934 to 1945 a total of 410 patients were admitted to University College Hospital with antepartum haemorrhage (2.7 per cent). However, these figures are too small to allow of any deduction being made as to whether fibroids predispose to this complication.

MYOMECTOMY.

This operation was attempted only 5 times. Two were performed for red degeneration, 2 for large fibroids (which had been diagnosed as ovarian cysts) and 1 on a fibroid which was thought likely to interfere with uterine growth later on.

Two patients had healthy babies delivered with forceps, one 5 weeks premature and the other at term. Another aborted one month after her operation and one (whose operation was done for necrobiosis) was not seen again after her discharge from hospital. The fifth bled so copiously at operation that it was necessary to perform a hysterotomy before the haemorrhage could be controlled.

The risk attached to the operation is about 0.5 per cent greater during pregnancy,[11] and its performance is rarely necessary. Watson[5] attempted it 3 times in 157 cases; 1 patient aborted, hysterotomy was necessary to control haemorrhage in a second, while a third went to term. Mussey and Hardwick[2] found that 12 of their 32 patients aborted and another died. Gemmell[16] collected 475 cases; 65 of these miscarried and 14 died.

TERMINATION OF PREGNANCY.

Hysterectomy was performed in 6 cases before the foetus was viable. On 4 occasions the pregnancy had not been diagnosed, irregular bleeding, amenorrhoea in middle-aged women and an ovarian cyst all helping to obscure its presence. Severe epilepsy and psychological reasons necessitated the other 2 operations.

Another pregnancy was terminated for severe thyrotoxicosis. Reference has been made already to the occasion on which hysterotomy was necessary to control severe haemorrhage during a myomectomy.

Summary of Complications During Pregnancy.

Total number of cases 122.

	No. of cases	Per cent
Normal pregnancy	49	40
Threatened abortion	12	9.8
Abortion	17	14
Premature labour	10	8.2
Red degeneration	22	18
Antepartum haemorrhage ...	5	4.1
Myomectomy	5	4.1
Termination	8	6.6

EFFECTS OF FIBROIDS ON LABOUR.

Of the 122 cases described above, 9 were not delivered by the hospital, 17 aborted and 8 were terminated. Of the remaining 88 cases, 50 had normal labours (57 per cent) although 7 of them were premature.

Primary Uterine Inertia. Eight cases (9.1 per cent).

Primary uterine inertia is defined here in an arbitrary manner as a first stage of labour lasting for more than 48 hours. It is possible that the prolongation of the first stage could have been due to other causes, such as rigid cervix, but these factors cannot be assessed from the case records.

Four cases had a primary uterine inertia in this sense and were later delivered normally, and 3 cases were delivered by Caesarean section after a similar time. Another patient was treated by Caesarean section as the membranes had ruptured 36 hours before, and she had weak pains.

Second Stage of Labour Lasting 3 Hours or More.

This complication was found in 8 patients (9.1 per cent), and no case was caused by an obstructing fibroid.

Pierson[4] notes "inertia" in 34.6 per cent of cases and "prolonged labour" in 16.8 per cent, but he does not define these

terms. However, in the present series it will be noted that 18 Caesarean sections in addition to those 4 cases noted were performed for various reasons (22 in all, or 25 per cent). It is possible a certain proportion of them would have developed inertia if they had been allowed to go through a normal labour. In Pierson's series the incidence of Caesarean section was only 14.6 per cent.

Forceps Deliveries.

It was necessary to extract 11 infants with forceps (12.5 per cent). Delay in the second stage, myomectomy during pregnancy and " deep transverse arrest " were the indications for their use.

A forceps delivery was necessary in 20 of the 101 patients recorded by Pierson[4] (20 per cent).

Caesarean Section.

Twenty-two patients were delivered by Caesarean section (25 per cent) and this figure resembles that recorded by Watson,[5] 35 operations in 157 patients (22.3 per cent). The most frequent indications were the patients' age, uterine inertia, an unfavourable presentation and an obstructing fibroid, but on one occasion an antepartum haemorrhage, twice a pre-eclampsia, once an ovarian cyst and once foetal distress in the first stage of labour added to this list.

During the operation, myomectomy was performed on 4 occasions, a procedure condemned by Browne[3] (except under certain circumstances), and a hysterectomy once.

Postpartum Haemorrhage (a vaginal loss of more than 20 ounces of blood).

Of the 66 patients who were delivered *per vaginam*, 2 patients had postpartum haemorrhage (3 per cent), and 1 manual removal of placenta was necessary (1.5 per cent). Pierson[4] has a far more gloomy

story to tell, 33.6 per cent of his patients having had postpartum haemorrhage. Polak[10] also noted a high incidence of haemorrhage, which occurred in 25 per cent of the cases he collected. Harris[17] thought haemorrhage was likely to occur only if the placenta were implanted over the fibroid, which might thus interfere with placental separation and uterine retraction. Watson had only 3 cases in his series of 157 (1.9 per cent), and two adherent placentae (1.3 per cent).

Malpresentations.

There were 6 breech (1 in a twin pregnancy) and 2 shoulder presentations at term. This is a very low incidence of malpresentation compared with other records.

Craniotomy.

One patient was admitted as an emergency in the second stage of labour. She was febrile, the foetus was dead, and a fibroid obstructed its delivery. A craniotomy was performed and the child extracted but the patient died about 6 weeks later. Munro Kerr[11] condemns dragging a child past an obstructing fibroid, but the alternative abdominal approach was thought to carry an even greater risk.

PUERPERIUM.

Morbidity was noted in 7 patients, but in only 2 instances could the temperature be attributed to the presence of the fibroids— 1 was due to red degeneration, and the other to a sloughing submucous fibroid.

Nearly all fibroids tend to diminish after delivery to their original size. Some authorities think that they may become smaller than before or even disappear, and they suggest that this phenomenon follows degeneration with liquefaction during pregnancy, and subsequent absorption of the fluid. One patient in University College Hospital was found to have fibroids

in 2 pregnancies, but no evidence of their presence was found in a third. However, Munro Kerr[11] and F. J. Browne[3] both doubt whether fibroids disappear completely.

Involution is said to be slower and the lochia to persist longer. Records were not available to confirm these findings.

One case of sloughing fibroids has been described already. Uterine inversion was not encountered. Spencer recorded this accident.[18]

MATERNAL DEATHS.

Three of the patients died, 1 from postoperative shock following a Caesarean section, 1 from a paralytic ileus 3 days after a Caesarean section and myomectomy, and the other from a terminal bronchopneumonia complicated by a vesicovaginal fistula and sloughing fibroids after craniotomy.

Summary of Complications During Labour.

Total number of cases 88.

	No. of cases	Per cent
Prolonged 1st stage of labour ...	8	9.1
Prolonged 2nd stage of labour ...	8	9,1
Forceps deliveries	11	12.5
Caesarean section	17	19.3
Caesarean section and myomectomy	4	4.5
Caesarean section and hysterectomy	1	1.1
Post-partum haemorrhage* ...	2	3.0
Manual removal of placenta* ...	1	1.5
Craniotomy*	1	1.5

* Only 66 patients were delivered *per vaginam*

INFANT REPORT.

Eighty children were discharged healthy from the hospital, one set of twins included.

Ten children were lost for the following reasons:

1. Five infants were born macerated. This figure includes another set of twins born in the 30th week.

2. One dead birth—it showed no signs of life after a premature labour complicated by a prolapsed cord in the 29th week.

3. Two stillbirths, where the cord was pulsating, but no attempts at respiration took place, occurred. One followed a manual dilatation of the cervix and forceps delivery for a prolonged first stage of labour, and the other a breech extraction.

4. There were 2 neonatal deaths. One followed a premature labour at the 28th week, and the other a forceps delivery following a prolapsed cord in the 34th week.

A number of authorities have pointed to the high foetal mortality-rate. Pierson[4] recorded one of 35.6 per cent, and Mussey and Hardwick[2] one of 28.9 per cent, but only 6.6 per cent where the child was viable. In his 157 cases, Watson[5] found 18 stillbirths and 2 intra-uterine deaths (12.7 per cent).

2. The incidence was 0.79 per cent, and the average age was 34.3 years.

3. More than 20 per cent of the patients were primigravidae of 36 years of age or more.

4. Pregnancy was normal in only 40 per cent of patients. The abnormalities have been described.

5. Labour was uncomplicated in 57 per cent of the cases and operative interference was frequently necessary; 12.5 per cent of the infants were extracted with forceps; Caesarean section was performed in 25 per cent of cases and craniotomy once.

6. The incidence of uterine inertia, although far greater than in unselected cases, was a less frequent complication than might have been expected from a study of other records.

7. Two cases only of morbidity could be attributed to the presence of fibroids.

8. There were 3 maternal deaths all resulting from operative interference.

SUMMARY OF FOETAL MORTALITY.

The stillbirth and neonatal death-rate was 11.1 per cent.

(The stillbirth and neonatal death-rate for all cases delivered by the hospital from 1935 to 1945 was 6.5 per cent.)

Total number of pregnancies	No. of healthy children born	Percentage of children lost (Abortions, stillbirths and neonatal deaths)
122−9*=113 (Two twin pregnancies included)	80 =69.6 per cent	30.4 per cent

* Nine patients not delivered by hospital.

SUMMARY.

1. One hundred and twenty-two cases of fibroids in pregnancy have been described, and their complications compared with those found by other observers.

9. Of the 113 patients who were looked after by the hospital, 79 only had healthy children. A large number aborted (14 per cent) and the foetal and neonatal death-rate was 11.1 per cent.

CONCLUSIONS.

1. The frequency of complications in pregnancy, labour and puerperium, and the high foetal and maternal death-rate show that the presence of fibroids is a serious complication.

2. Red degeneration during pregnancy should be treated conservatively and myomectomy should, if possible, be avoided.

3. Caesarean section will usually secure a living child, and it should be seriously considered in all elderly primigravidae and all other patients where there is an additional complication.

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A Statistical Study on the Effects of Exercises on Childbearing

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INTRODUCTION.

THE object of this study was to determine what apparent effect the regular practice of special exercises during pregnancy had upon the patient during her confinement, and how the labour of exercise patients compared with that of a group of controls. The material used for this study consisted of the case notes of 340 primiparous women who had received regular instruction in prenatal and labour exercises from the 16th to the 20th week to the end of the end of the pregnancy and a control group of 340 primiparous women who had not received such special instruction nor practised special exercises. Patients included in this study attended classes at the antenatal clinic at intervals of 2 weeks and practised the exercises at home.

In labour, the patients attempted to carry out the exercises they were taught during pregnancy, but there was no supervision by the physiotherapist. The midwives responsible for the supervision of the patients were able to spend very little time with them during the first stage of labour, with the result that the benefit of antenatal preparation of the patient for labour was not felt as much as had been hoped.

The special postures advocated by some teachers of labour exercises were not taken up by patients in the series of cases studied. In cases of normal labour patients were encouraged to walk about during the first stage of labour; in the second stage the dorsal position was adopted and for delivery the left lateral position.

OBSERVATIONS ON THE PURPOSE AND PRACTICE OF PRENATAL AND LABOUR EXERCISES.

During pregnancy and labour the structures of the body, particularly the muscles of the abdomen and spine and the joints and ligaments of the pelvis and the tissues of the pelvic floor are subjected to considerable strain, and as a result many women are left with disabilities which cause much discomfort and ill-health. It appears that at least some of the disabilities following childbirth might be avoided if there was a greater appreciation of the mechanics of the body and a better understanding by the patient of muscle control and co-ordination of movement and of the principle of mental and physical relaxation.

Little attention has so far been given to the study of the mechanics of the body in pregnancy and labour, but considerable attention is now being given to the subject of educating the expectant mother in the control and use of her muscular system, and great eagerness is usually shown by her in practising what she is taught, because she believes that her labour will be made easier by such practice.

Prenatal exercises and exercises for the confinement are now taught at many clinics of maternity units and hospitals and also in private midwifery practice. Those responsible for the training are usually physiotherapists who have themselves undergone special training in maternity exercises. The systems practised show

surprising variations and not all exercises taught and practised have a scientific basis. The frequency of the instruction is often not sufficient to ensure that the patient has mastered the principle of the exercises before she goes into labour and in such cases the cause of labour may be hindered rather than helped.

PURPOSE OF THE EXERCISES.

Prenatal Exercises.

The object of these exercises is

(a) To teach the expectant mother the basic principles of muscle control, of mental and physical relaxation and how to use her muscles effectively in her daily work, exercise and labour.

(b) To help her to adopt and maintain a good posture during pregnancy as the size and weight of the uterus increases, and to lessen the fatigue and backache usually associated with increasing lordosis.

(c) To improve the circulation and muscle tone, by the practice of deep breathing exercises and special exercises for the spinal, abdominal and pelvic floor muscles.

(d) To increase the flexibility of the pelvic joints.

Exercises for the Confinement.

These have been designed with the object of shortening labour, lessening fatigue and aiding natural childbirth.

For the first stage of labour the basic principle of teaching is muscular relaxation

TABLE I. INVESTIGATION OF LABOUR.

An Analysis of the Case Notes of 340 Exercise Patients and 340 Control Patients.

TYPE OF LABOUR.

	Exercise cases		Control cases		Presentation	Delivery	Third stage	Exercise cases		Control cases	
	No.	Per cent	No.	Per cent				No.	Per cent	No.	Per cent
Normal labour	253	74.4	245	72.1							
Abnormal labour	69	20.3	81	23.8	1. Vertex	Spontaneous	Recorded. haemorrhage 20 ounces or over	23	33.3	36	44.4
					2. Vertex	Forceps	Normal	29	42.0	27	33.3
					3. Vertex	Forceps	Recorded haemorrhage 20 ounces or over	9	13.0	9	11.1
					4. Breech	Assisted	Normal	8	11.6	8	9.9
					5. Face	Spontaneous	Recorded haemorrhage 20 ounces				
Premature labour	18	5.3	14	4.1			or over	—	—	1	1.2
Total	340	100.0	340	100.0			Totals	69	99.9	81	99.9

particularly during the phase of uterine contractions.

For the second stage the patient is taught: (a) to make effective use of her abdominal muscles and muscles of the diaphragm, to aid the expulsive contractions of the uterus, (b) to practise relaxation between uterine contractions in order to lessen the tendency to fatigue, (c) and to relax the muscles of the pelvic floor to ease the birth of the child. Another feature of the exercises, regarded as of first importance by some teachers, is the adoption of a special posture such as squatting, crouching or kneeling during labour and delivery. These primitive postures are not generally liked by midwives or mothers in this country who prefer the dorsal or left lateral position for childbirth, and for this reason the special postures have not been accepted in many of the teaching centres.

It will be seen from Table I that for the exercise group of 340 patients, labour was normal in 253 cases, or 74.4 per cent of the total; abnormal in 69, or 20.3 per cent; and premature in 18, or 5.3 per cent—2 of the latter group being the result of induction of labour.

In the control group of 340 patients, labour was normal in 245 cases, or 72.1 per cent of the total; abnormal in 81, or 23.8 per cent; and premature in 14, or 4.1 per cent.

The analysis shows approximately the same proportion of cases of normal, abnormal and premature labour in both the exercise and control groups.

PRESENTATION IN LABOUR.

(a) *Vertex presentation.* There were 314 or 97.5 per cent of cases of vertex presentation for the exercise group of 322 cases and 317, or 97.2 per cent for the 326 controls.

(b) *Breech presentation.* There were 8 cases of breech presentation in the 26 to 30 age group of the exercise cases and in addition 4 others in the over 30 age group in which version was performed between the 34th and 36th week of pregnancy—making a total of 12, or 3.7 per cent relative to the group total of 322.

In the control group there were 8 cases of breech presentation, 7 of which were in the 26 to 30 age group, and 3 others in which version was performed, making a total of 11, or 3.4 per cent relative to the group total of 326.

The presentation in late pregnancy and labour showed the same proportion of vertex presentations in both groups.

DETAILS OF LABOUR.

Spontaneous delivery.

Of the 314 exercise cases in which the vertex was presenting, there were 276, or 87.9 per cent of cases in which spontaneous delivery resulted, and of the 317 control cases 281, or 88.6 per cent.

The average duration of labour was about the same for the exercise and control groups of all ages (Table II).

VARIATIONS IN THE DURATION OF LABOUR IN CASES OF VERTEX PRESENTATION AND OF SPONTANEOUS DELIVERY AT OR NEAR TERM.

(a) 276 exercise cases; (b) 281 control cases.

Labour not Exceeding 24 hours.

In the exercise age group up to 30 years there were 172, or 78.9 per cent of cases in which the duration of labour did not exceed 24 hours and among the controls 154, or 70.9 per cent out of 217 cases. In the older groups of 31 years and above, there were 42, that is 72.4 per cent, out of a total of 58 exercise cases and 40, that is 62.5 per cent, out of a total of 64 cases.

TABLE II. AVERAGE DURATION OF LABOUR IN CASES OF VERTEX PRESENTATION AND OF SPONTANEOUS DELIVERY AT OR NEAR TERM.

(a) 276 Exercise Cases.   (b) 281 Control Cases.

Age group	Group	No. of cases	Stages of labour								
			First		Second		Third		Total	
			Hr.	Min.	Hr.	Min.	Hr.	Min.	Hr.	Min.
20 years and under	(a) Exercise	11	23	9	1	1	—	21	24	31
	(b) Control	11	17	31	—	56	—	19	18	46
21 to 25 years	(a) Exercise	95	17	48	1	19	—	21	19	28
	(b) Control	98	15	54	1	24	—	20	17	38
26 to 30 years	(a) Exercise	112	20	49	1	31	—	20	22	40
	(b) Control	108	21	5	1	37	—	24	23	6
31 to 35 years	(a) Exercise	52	17	47	1	41	—	21	19	49
	(b) Control	56	23	24	1	41	—	21	25	26
36 years and over	(a) Exercise	6	20	33	1	15	—	23	22	11
	(b) Control	8	19	41	1	59	—	21	22	1
All ages	(a) Exercise	276	20	1	1	21	—	21	21	44
	(b) Control	281	19	31	1	31	—	21	21	24

For all ages the figures were 214, that is 77.5 per cent, out of a total of 276 cases and for the controls 194, that is 69 per cent, out of a total of 281 cases.

The difference of 8 per cent more exercise cases than controls with labour not exceeding 24 hours for the 30 years and under group; 9.9 per cent for the 31 years and over age group; and 8.5 per cent more for all ages, certainly is a slight advantage to the exercise cases, but the figure is not large enough to be of significance.

ABNORMAL LABOUR.

FORCEPS DELIVERY.

There were 38, or 12.1 per cent of cases of forceps delivery relative to the 314 cases of vertex presentation at or near term in the exercise group and 36, or 11.4 per cent among the 317 controls.

The average total duration of labour was about the same in both exercise and control groups; it was considerably longer than for those cases where delivery was sponta-

TABLE III. AVERAGE DURATION OF LABOUR. FORCEPS DELIVERY.

(a) 38 Exercise cases; (b) 36 Control Cases at or Near Term.

Group	No. of cases	Stages of labour							
		First		Second		Third		Total	
		Hr.	Min.	Hr.	Min.	Hr.	Min.	Hr.	Min.
(a) Exercise ...	38	36	11	3	17	—	24	39	52
(b) Control ...	36	37	39	3	34	—	25	41	38

neous. For the exercise group it was 39 hours 52 minutes and for the controls 41 hours 38 minutes compared with 21 hours 44 minutes and 21 hours 24 minutes for cases of spontaneous delivery, showing a difference of 18 hours 8 minutes for the exercise group and 20 hours 14 minutes for the controls (Table III).

There was a difference of 1 hour 46 minutes between the total duration of labour in cases of forceps delivery for both groups.

account of delay due to mechanical difficulties and weak uterine contractions, and in 31 or a ratio of 82.6 per cent of the 36 controls (Table IV).

CASES OF BREECH PRESENTATION.

The number of cases of breech presentation at or near term was 8, or 2.5 per cent of the total of 322 exercise cases and 8, or 2.5 per cent of the 326 controls. In 4 other exercise cases version had been performed

TABLE IV.   ABNORMAL LABOUR.   FORCEPS DELIVERY.
Indications for the use of Forceps in Cases of Vertex Delivery at or Near Term.

Indications	Exercise cases		Control cases	
	Number	Percentage	Number	Percentage
Foetal distress	2	5.3	3	8.3
Cardiac condition	1	2.6	2	5.5
Mechanical difficulties:				
(a) Vaginal septum	1	2.6	–	–
(b) Disporportion—anterior position of foetus	4	10.5 .	6	16.6
(c) Posterior position of foetus...	12	31.6	11	30.6
(d) Deep transverse arrest of foetal head. Weak uterine contractions anterior position of foetus	11 7	29.0 18.4	5 9	14.0 25.0
Totals	38	100.0	36	100.0

A record of the position of the foetus was, in most cases, made after abdominal examination when the patient was admitted in labour, but in a number of cases the position was not determined. On this account we do not know in how many cases partial or complete rotation of the head had taken place.

The list of indications for the use of forceps is not really helpful, for the added factors of weak uterine contractions and disproportion contributed to delay in a number of the cases of posterior and lateral position of the foetus.

In 35 or a ratio of 92.1 per cent of the 38 exercise cases, forceps were applied on

between the 34th and 36th week of pregnancy and in 3 of the control cases. It appears probable that for the exercise group there would have been 12, or 3.7 per cent of cases of breech presentation and for the controls 11, or 3.4 per cent (Table V).

There is no indication that the practice of the special exercises had an effect on the presentation in late pregnancy.

The average total duration of labour was 14 hours 55 minutes for the exercise group of 8 cases of breech presentation and 19 hours 14 minutes for the controls.

In none of the exercise cases did labour exceed 24 hours, but in 3 of the controls it exceed 36 hours.

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TABLE V. CASES OF BREECH DELIVERY AT OR NEAR TERM.
AVERAGE DURATION OF LABOUR.
(a) 8 Exercise Cases; (b) 8 Control Cases.

| Group | No. of cases | Stages of labour | | | | | | | |
| | | First | | Second | | Third | | Total | |
		Hr.	Min.	Hr.	Min.	Hr.	Min.	Hr.	Min.
(a) Exercise ...	8	12	54	1	41	–	19	14	55
(b) Control ...	8	17	14	1	33	–	27	19	14

PREMATURE LABOUR.

The number of cases of premature labour was 18, or 5.3 per cent relative to the total of 340 cases in the exercise group and 14, or 4.1 per cent of the 340 in the control group. Among the exercise cases there were 2 of induced labour for pre-eclamptic toxaemia; one case of toxaemia not induced; 2 of hyperpiesis; and 1 of twins. Among the control cases there were 2 of pre-eclamptic toxaemia; 1 of lateral placenta praevia; 1 of influenza preceding the onset of labour; and 5 of twins. Control of labour was not induced in any of the cases. No cause was found for the onset of premature labour in the remaining 8 exercise and 5 control cases.

There is no difference in the incidence of prematurity in the 2 groups.

PREMATURE BIRTHS.

FOETAL AND INFANT MORTALITY.

In the exercise group of premature births there were 3 stillbirths, one due to a toxaemic condition of the mother, another was a result of a complication of labour and the third a hydrocephalic foetus weighing 1 pound 12 ounces. In the control group there were 4 stillbirths—one due to a toxaemic condition of the mother, another to a true knot in the umbilical cord and 2 twins for whom the cause of foetal death was not known.

SEDATIVES AND ANALGESICS.

ADMINISTERED DURING LABOUR.

Sedatives and analgesic drugs administered during the first stage of labour were

TABLE VI. AVERAGE DURATION OF PREMATURE LABOUR.
(a) 18 Exercise Cases; (b) 14 Control Cases.

| Group | No. of cases | Stages of labour | | | | | | | |
| | | First | | Second | | Third | | Total | |
		Hr.	Min.	Hr.	Min.	Hr.	Min.	Hr.	Min.
(a) Exercise ...	18	18	34	1	5	–	15	19	55
(b) Control ...	14	12	8	1	52	–	20	14	20

The average total duration of premature labour in the 18 exercise cases was 19 hours 55 minutes and for the controls 14 hours 20 minutes. In 2 cases of twins and 3 other cases in the exercise group, labour exceeded 24 hours, and in 2 cases of twins and 1 other in the control group (Table VI).

potassium bromide, chloral hydrate, tincture of opium and morphine sulphate.

In the exercise group of patients, 1 or more of these drugs in single or repeated doses were given to 171, that is 50.3 per cent of patients and in the control group to 146, that is 42.6 per cent. The analgesic

drugs, tincture of opium and morphine, were administered in 15 per cent of cases in both groups.

In the second stage of labour gas and air analgesia was administered for all normal cases where conditions were suitable and the length of the second stage allowed for its administration, except in a rare case in both the exercise and control groups where the patient expressed the wish not to have the analgesia administered so that she might be assured that she was co-operating fully in the birth of her baby.

There was no evidence that labour was less painful for those patients who had practised the exercises than for those who had not done so.

POSTPARTUM HAEMORRHAGE.

Among the exercise group of 276 cases of vertex presentation with spontaneous delivery, there were 23, or 8.3 per cent in which postpartum haemorrhage of 20 ounces or more was recorded and in the control group of 281 cases there were 36, or 12.8 per cent.

Among the 38 exercise cases delivered by forceps, there were 9, or 23.7 per cent in which postpartum haemorrhage of 20 ounces or more was recorded and in the control group of 36 cases 9, or 25 per cent.

In the premature group of exercise cases, 3 cases of excessive haemorrhage were recorded and in the control group 2 cases. Of these, 2 in both groups were cases of twins.

PERINEAL LACERATIONS.

(a) 276 exercise cases; (b) 281 control cases.

Among the 276 cases of vertex presentation with spontaneous delivery at or near term, there were 166, or 60 per cent of cases with perineal lacerations in the exercise group and 158, or 56.2 per cent in the control group.

Episiotomy was performed in 2 of the exercises cases and 6 of the controls of the under 30 age groups.

AVERAGE BIRTH-WEIGHT OF INFANTS.

For the exercise group of 322 cases delivered at or near term, the average birth-weight for the male infants was 7 pounds 7 ounces, and for the females 7 pounds 2 ounces. For the control group of 326 cases the average birth-weight for the male infant was 7 pounds 6 ounces and for the female 7 pounds 3 ounces. The average weight in both groups for male and female was 7 pounds 4½ ounces.

The average birth-weight of the premature infants in the 18 exercise cases was 4 pounds 9 ounces for the male infants and for the females 4 pounds 14 ounces. For the control group the average weight of the males was 5 pounds 1 ounce, and for the females 4 pounds 10 ounces. The average for males and females in both groups was 4 pounds 11½ ounces, and 4 pounds 9½ ounces for the controls.

FOETAL AND INFANT MORTALITY.

Among the exercise group of 322 cases delivered at or near term, there were 8, or 2.4 per cent stillbirths and 1 infant death. Two of the stillbirths were associated with hydrocephaly, 1 with toxaemia of the mother, another was due to a congenital heart lesion; 3 were the result of complications of labour and in 1 case the cause was not known. The infant death was due to atelectasis.

In the control group of 326 cases, there were 7 or 2.2 per cent stillbirths, 3 of which were due to complications of labour; 1 other due to haemolytic disease; and in 2 cases the cause was not known.

There were 2 infant deaths, 1 due to cerebral haemorrhage following a breech delivery and the other to congenital malformation of the heart.

The total number of stillbirths, including the 3 premature stillbirths, was for the exercise group 11, or 3.2 per cent of 344 births and for the control group of 345 births 12, or 3.4 per cent, including the 4 premature births.

SUMMARY AND CONCLUSIONS.

1. An analytical study has been made of the obstetric case notes of 340 primiparous women who had received instruction in maternity exercises and of a comparative group of controls.

2. *Type of labour.* The cases were divided into 3 groups, those of normal labour, abnormal and premature labour.

In the exercise group there were 253, or 74.4 per cent of cases of normal labour, 69, or 20.3 per cent of abnormal and 18, or 5.3 per cent of cases of premature labour. For the controls there were 245, or 72.1 per cent of cases of normal labour, 81, or 23.8 per cent of abnormal and 14, or 4.1 per cent of cases of premature labour.

(In the exercise group 2 of the cases of premature labour were the result of induction.)

The proportion of cases in each group is approximately equal for both exercise and control cases.

3. *Presentation.* There were 314, or 97.5 per cent of cases of vertex presentation for the exercise group of 322 cases, and 317, or 97.2 per cent for the 326 controls, and 8, or 2.5 per cent of cases of breech presentation for both groups.

4. *Delivery.* Spontaneous delivery occurred in 276, or 87.9 per cent of the 314 cases in the exercise group, and in 281, or 88.6 per cent of the 317 cases in the control group.

5. The average duration of labour in cases of vertex presentation and of spontaneous delivery at or near term was for the 276 exercise cases 21 hours 44 minutes, and for 281 control cases, 21 hours 24 minutes.

6. The number of cases in the above 2 groups in which labour did not exceed 24 hours was, for the exercise cases, 214, or 77.5 per cent, and for the controls 194, or 69 per cent.

The slight difference of 8.5 per cent more cases for the exercise group is not enough to be regarded as a significant figure.

7. *Forceps delivery.* The number of cases of forceps delivery was 38, or 12.1 per cent relative to the 314 exercise cases of vertex presentation and 36, or 11.4 per cent of the 317 controls.

8. The average duration of labour in cases resulting in forceps delivery was 39 hours 52 minutes in the exercise group and 41 hours 38 minutes in the control group. This was 18 hours 8 minutes longer than for cases of spontaneous delivery for the exercise cases and 20 hours 14 minutes longer for the controls.

9. *Indication for the use of forceps.* In 35, or a ratio of 92.1 per cent of 38 exercise cases, forceps were applied on account of delay due to mechanical difficulties and weak uterine contractions and in 31, or a ratio of 86.2 per cent of the 36 controls.

10. *Breech presentation.* Among the exercise group there were 8, or 2.5 per cent in the 322 exercise group, and the same number among the controls. (Version had been performed in 4 other exercise cases and 3 controls.)

11. *Premature labour.* The number of cases of premature labour was 18, or 5.3 per cent relative to the total of 340 exercise cases and 14, or 4.1 per cent for the controls. (Among the exercise cases there were 2 of induced labour.)

12. The average duration of premature labour was 19 hours 55 minutes for the

exercise group and 14 hours 20 minutes for the controls. This is an appreciable difference in favour of the controls, but the number of cases is so small that it would be erroneous to regard the figure as of any significance.

13. *Premature stillbirths.* There were 3 in the exercise group and 4 among the control group.

14. *Sedatives and analgesia.* These were administered in 171, or 50.3 per cent of exercise cases and 146, or 42.6 per cent of controls. Analgesic drugs were given in 15 per cent of cases in both groups. Gas air analgesia was given to almost all the patients in both groups.

15. *Postpartum haemorrhage.* Among the exercise group there were 23, or 8.3 per cent of recorded cases of postpartum haemorrhage in the exercise group of 276 cases of spontaneous delivery, and 36 or 12.8 per cent among the control group of 281.

16. *Perineal lacerations.* Among the 276 exercise cases of spontaneous delivery there were 166, or 60 per cent with perineal lacerations and among the 281 controls 158, or 56.2 per cent.

17. *Average birth-weight of infants.* This was 7 pounds 4½ ounces for both exercise and control groups.

18. *Foetal and infant mortality.* The number of stillbirths among the exercise group of 322 cases delivered at or near term was 8, or 2.4 per cent, compared with 7, or 2.2 per cent of the 326 cases among the control group. There was 1 infant death in the exercise group and 2 in the control group.

This detailed study has not revealed any appreciable difference between the exercise and control groups for the type of labour, presentation, average duration of labour, for postpartum haemorrhage and perineal lacerations, for the average weight of infants and infant mortality rates. There is no indication from this analysis that labour was less painful for the exercise cases than for the controls.

It appears that the infrequency of the instruction and the lack of supervision in labour by a trained instructress lessened the value of the antenatal training.

More trained persons are needed before the value of maternity exercises in preparation for childbirth can be properly assessed. This aspect of antenatal work can only be fully developed when all midwives and pupil midwives are trained in the principles of the exercises; understand the objects of their practice and encourage the patient to carry them out during pregnancy and labour.

Timing of Endometrial Biopsy

BY

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In the investigation of sterile matings the problem of when best to collect a fragment of endometrium for biopsy is a real one. Obviously to obtain a fair estimate of the full degree of progestational development reached by the endometrium the nearer to the onset of menstruation the material for biopsy is obtained the better, though much of interest can be learnt from biopsies taken at earlier stages in the cycle. There is always a difficulty, considerable in private, and greater still in clinic or hospital practice, when there may be only 1 or 2 days in a week to choose from, in estimating on what date to arrange an appointment for this examination. This particularly applies to patients with irregular cycles. One solution is deliberately to give a rather too early appointment telling the patient to return each week for another biopsy until menstruation starts. An alternative method of attempting to surmount the difficulty is to see the patient immediately after the onset of menstruation; but this, which entails an appointment at short notice, is by no means convenient to arrange in a busy private or hospital practice; moreover, many women dislike being examined and subjected to any extra discomfort during a period. Those who advocate doing a biopsy on the 1st day of menstruation claim the added advantage that there is no danger of disturbing a possible conception. This fear, far from being confirmed, has, in my experience been very largely removed by the not uncommon observation that patients fail to report another period after the taking of endometrium for biopsy. It seems indeed that this procedure tends in certain cases to encourage successful embedding rather than to disturb the early embryo.

In a series of some 850 subfertile matings this absence of subsequent menstruation has now been noted in at least 35 cases where follow-up has been possible. These cases are summarized in Table I, together with 1 case that can be classified as fertile. With the exception of this case all these patients came for advice because of difficulty in conceiving or carrying a pregnancy to term. All the biopsies were obtained without anaesthesia in clinic or consulting room. The average age of the 35 subfecund women was 30 years (youngest 19 years, oldest 41 years); they had, on an average, been trying to become pregnant for 2 years (shortest time 3 months, longest $4\frac{1}{2}$ years) before being seen; 19 had not had a previous pregnancy; 5 had each had 1 child born alive; 2 had had 1 live birth and 2 miscarriages; 1 had had 1 stillbirth and 1 child born alive; 1 had had 1 stillbirth; 1 had had a stillborn infant and 2 miscarriages; 2 had had 1 miscarriage; 2 had had 2 miscarriages; 1 had 3 and 1 had 4 miscarriages. The remaining patient, who was not infertile, had had 1 live birth previously. In 17 of the infertile cases, except for routine pelvic examination,

FIG. 1

CASE 20. 11th day of cycle. Subnuclear
vacuolation seen.   × 100

FIG. 2

CASE 27. 23rd day of cycle. Changes
correspond to later date.   × 100

FIG. 3

CASE 31. 24th day of cycle. Advanced
changes.   × 100

M. H.-J.
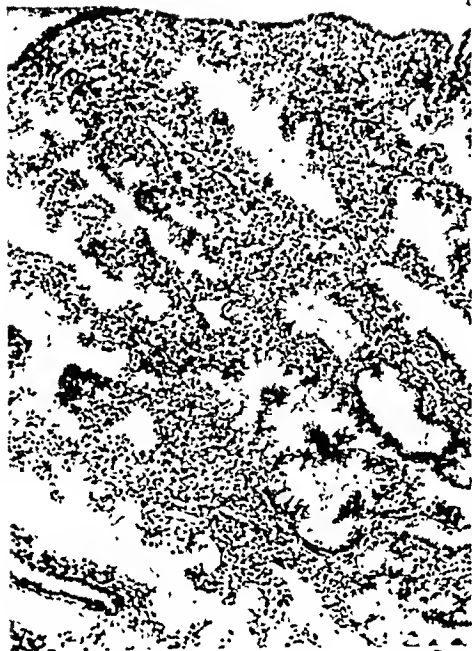
FIG. 4

CASE 28.   25th day of cycle.   Advanced
changes.   × 100
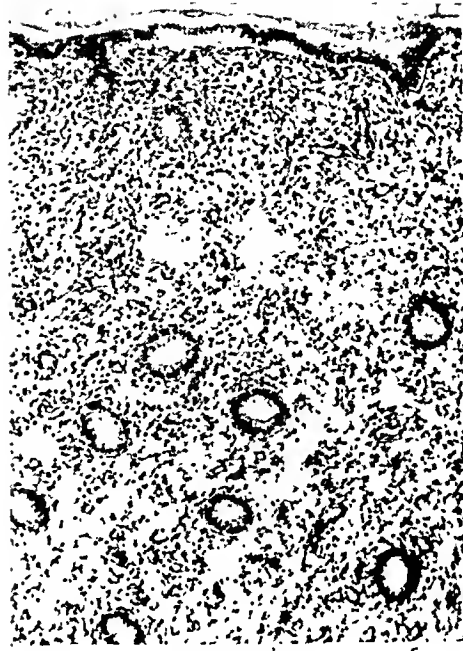

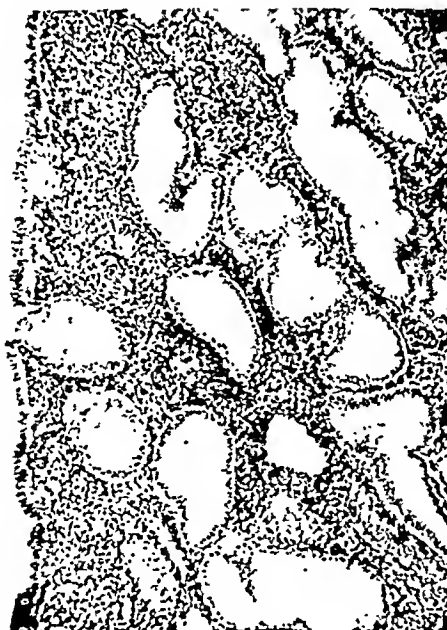FIG. 5

CASE 21.   14th day of cycle.   Changes
delayed.   × 100

FIG. 6

CASE 4.   25th day of cycle.   Changes
delayed.   × 100

M. H.-J.

endometrial biopsy was the only procedure carried out and no treatment was given before the cycle in which pregnancy occurred. In 14 cases a tubal insufflation had been done either before, or at the same time as the critical biopsy and 5 of these and the 4 remaining infertile patients had received treatment of one sort or another (endocrines, pelvic diathermy, cauterization of the cervix, etc.) before the cycle in which the critical biopsy was done. Thirty-seven biopsies are included in the series, as in 1 case a biopsy was taken on two occasions in the same cycle as that in which conception occurred. Seven of the biopsies were done before the 14th day, that is in the first half of the cycle and most probably before ovulation had occurred; 30 were taken on or after the 14th day of the cycle and 18 of these between the 25th and 35th day, therefore probably after embedding had started. The microscopical appearance corresponded on the whole with what would be expected for the days in the cycle when the biopsies were taken, except in a few cases where the stage of development was either rather more or less advanced than might have been expected. For example, the biopsy taken on the 11th day of the cycle in case 20 (Fig. 1) shows some subnuclear vacuolation, and in those taken on 23rd, 24th and 25th days in cases 27 (Fig. 2), 31 (Fig. 3), and 28 (Fig. 4) the glands are markedly tortuous, secretion is plentiful and there is some pre-decidual change in the stroma; in fact, these 3 sections are comparable to some of those taken more than a week later. On the other hand, the biopsies taken on the 14th and 25th days in cases 21 (Fig. 5) and 4 (Fig. 6) are apparently at least a week behind in their development.

It may be noted that the greatest variations in degree of development is found in those biopsies taken between the 21st and 26th days of the cycle.

Of the 36 pregnancies which started in the cycles when these biopsies were obtained, 22 are known to have gone to full time with the delivery of normal, living infants (13 male, 8 female and 1 sex unrecorded); 1 ended prematurely with the delivery of a macerated female foetus; 4 ended in spontaneous miscarriages at between 2 and 5 months; 8 are at present pregnant; and 1 pregnancy was terminated for medical reasons at $2\frac{1}{2}$ months. The last case is the only one that can be described as fully fertile; the biopsy was done for diagnostic purposes on the 34th day of the cycle and revealed a full blown (pro)gestational endometrium; the pregnancy continued uninterrupted, but unfortunately the patient's condition necessitated therapeutic abortion. The case that produced a macerated foetus at 8 months had had 2 previous miscarriages at $2\frac{1}{2}$ and 3 months and subsequently achieved a slightly premature live infant. Of the cases that miscarried between 2 and 5 months, 2 had not previously been pregnant in spite of having practised coitus without contraception for more than a year, and both subsequently conceived again with very little trouble and have been delivered of full-time live infants. The 2 remaining cases had previously had 3 and 4 miscarriages each and on this occasion carried farther than they had in any of those previous pregnancies; 1 had an attack of influenza and bronchitis with considerable pyrexia and treatment with sulphanilamide just before she miscarried; the other developed a toxaemia which progressed in spite of treatment and ended with the expulsion of a slightly macerated foetus at the 5th month.

Whether one must regard the occurrence of pregnancy following upon the taking of endometrium for biopsy in all these 35 subfecund women as purely fortuitous is a moot point. The well-recognized pheno-

TABLE I.

Case	Age	Years married Yrs.	Mths.	No contraceptives used before seeking advice Yrs.	Mths.	Previous pregnancies	Dates of L.M.P.	Dates of Biopsy	Day in cycle	Histology	Tubal insufflation	Treatment before date of biopsy	Result
1	35	1	0	1	0	0	13.8.41	10.9.41	29	Secretory late			L.B. ♂ 25.5.42
2	35	5	0	4	6	0	15.10.41	24.10.41	10	Follicular	Yes		L.B. ♂ 10.8.42
3	34	5	0	2	0	0	20.9.42	25.9.42	6	Follicular	Yes	Yes	Misc. 3 months 7.11.42
4	22	3	8	3	6	0	21.12.42	15.1.43	25	Secretory mid			L.B. 3.10.43
5	25	1	6	0	8	0	14.2.43	11.3.43	25	Secretory mid	Yes	Yes	L.B. ♂ 22.11.43
6	26	3	4	1	6	0	15.3.43	23.3.43	9	Follicular	Yes		L.B. ♂ 20.12.43
7	28	4	6	1	0	0	3.5.43	10.5.43	8	Follicular Some subnuclear vacuolation	Yes		L.B. ♀ 22.2.44
8	37	1	3	1	0	0	17.5.43	24.5.43	8	Follicular rather atrophic			L.B. ♀ 28.2.44
9	35	8	0	4	0	0	15.8.43	13.9.43	30	Secretory late	Yes	Yes	L.B. ♀ 17.6.44
10	34	5	0	0	3	3 misc.	3.12.43	3.1.44	32	Secretory late			Misc. 5 months 4.5.44
11	19	1	5	1	0	1 misc.	24.12.43	28.1.44	35	Secretory late			L.B. ♀ 13.9.44
12	28	3	6	1	6	1 S.B.	31.12.43	31.1.44	31	Secretory late			L.B. ♂ 5.10.44
13	34	8	0	4	0	1 L.B.	1.3.44	14.3.44 28.3.44	14 28	Ovulatory Secretory late			L.B. ♀ 6.12.44
14	34	8	0	0	0	1 L.B.	15.3.44	18.4.44	34	Secretory late			Surgical induction at 2½ months
15	25	5	0	2	0	0	14.4.44	18.5.44	34	Secretory late			L.B. ♀ 23.1.45
16	22	2	6	0	3	2 misc.	16.6.44	27.6.44	12	Follicular			Prem S.B. ♀ 10.3.45
17	37	6	8	4	0	1 L.B.	6.9.44	19.9.44	14	Ovulatory	Yes		L.B. ♂ 30.5.45
18	29	3	2	3	0	0	5.9.44	25.9.44	21	Secretory early	Yes		L.B. ♂ 27.6.45

TABLE I (Continued)

Case	Age	Years married Yrs.	Mts.	No contraceptives used before seeking advice Yrs.	Mts.	Previous pregnancies	Dates of L.M.P.	Biopsy	Day in cycle	Histology	Tubal insufflation	Treatment before date of biopsy	Result
19	32	4	6	2	0	2 misc.	26.9.44	9.10.44	14	Ovulatory		Yes	L.B.♂ 12.7.45
20	27	2	6	?		4 misc.	28.10.44	7.11.44	11	Ovulatory		Yes	Misc. 5 months 1.3.45
21	34	7	0	0	3	1 L.B. 2 misc.	25.11.44	8.12.44	14	Follicular late or just ovulatory			L.B.♂ 19.8.45
22	29	5	6	0	4	1 S.B. 2 misc.	29.11.44	21.12.44	23	Secretory early			L.B.♂ 22.9.45
23	32	5	9	0	4	0	16.1.45	9.2.45	25	Secretory mid		Yes	L.B.♂ 28.10.45
24	41	7	0	2	0	1 L.B. 2 misc.	24.2.45	16.3.45	21	Secretory mid			L.B.♂ 15.11.45
25	22	1	0	1	0	0	5.3.45	5.4.45.	32	Secretory late	Yes	Yes	Misc. 5 months 5.8.45
26	34	4	10	2	6	0	20.5.45	12.6.45	24	Secretory mid	Yes		L.B.♀ 27.2.46
27	26	4	10	1	2	1 L.B. 1 misc.	1.11.45	23.11.45	23	Secretory mid		Yes	L.B.♂ 1.8.46
28	27	1	3	0	6	1 misc.	27.11.45	21.12.45	25	Secretory late			•L.B.♀ 6.9.46
29	21	2	6	0	2	0	13.1.46	8.2.46	27	Secretory late			8½ mts. pregnant now
30.	31	8	0	3	0	0	22.4.46	17.5.46	26	Secretory late			5½ ,,
31	32	7	0	1	6	0	28.5.46	20.6.46	24	Secretory mid or late	Yes		4 ,,
32	36	14	0	2	0	{ 1 S.B. 1 L.B.	30.5.46	21.6.46	23	Secretory mid	Yes	Yes	4 ,,
33	33	5	8	1	6	1 L.B.	14.6.46	11.7.46	28	Secretory late	Yes		3 ,,
34	36	12	6	0	10	1 L.B.	16.6.46	12.7.46	27	Secretory late	Yes	Yes	3 ,,
35	21	2	6	2	3	0	30.6.46	26.7.46	27	Secretory late			3 ,,
36	29	5	3	0	6	0	10.8.46	2.9.46	23	Secretory early or mid.			2 ,,

menon of deciduoma-formation following traumatization of the endometrium in animals suggests that it may be something more than chance and that the slight trauma inflicted by obtaining a biopsy may in fact have a mildly therapeutic effect.

SUMMARY.

A short series of cases is described in which material for endometrial biopsy was obtained in the same cycle in which conception occurred without apparently interfering with the pregnancy.

Coarctation of the Aorta in Association with Pregnancy

(A Review of the Literature with Description of a Case)

BY

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ALTHOUGH coarctation of the aorta is such a well-defined and well-recognized congenital lesion, its association with pregnancy is remarkably uncommon. The literature of this country contains few references to the management of such cases, and no comprehensive review. Fawcett,[1] Weber and Price,[2] Gossage,[3] and Evans,[4] each reported 1 case of coarctation of the aorta in women who had borne children, and Maxwell,[5] Bramwell and Longson,[6] Walker,[7] and Billinghurst,[8] have described the course of pregnancy in women with this congenital abnormality, making 8 reported British cases. Several reviews of the subject have appeared in the American literature. Mendelson[9] summarized the reported case histories of 26 women with coarctation who had had children, and added 3 cases of his own. Kinney, Sylvester and Levine[10] reported another case of coarctation in a pregnant woman, and listed in addition 9 new cases from the literature, bringing the total number to 39. This catalogue includes all the reported British cases except that of Billinghurst, which appears to have escaped the reviewers' attention. We have 1 case of our own, and know of 2 cases as yet unpublished, so that with these 3 cases to be described the total stands at 43.

The paucity of cases is at first sight surprising, but coarctation of the aorta is an abnormality which is distinctly more common in males than females. Maud Abbott,[11] in her series of 200 cases in subjects over 3 years of age, found 48 females (147 males, 5 sex unknown). Six of these females became pregnant, and their histories were described by Leudet,[13] Kreigh,[14] Fawcett,[1] Abbott,[12] Katz,[15] and Strassman.[16] The incidence of pregnancy is strikingly low, as most of the 48 patients were women of childbearing age.

MANAGEMENT OF THE INDIVIDUAL CASES.

The occurrence of pregnancy in a patient with coarctation must constitute a certain hazard, but there is a divergence of opinion about the severity of the risk. Opinions must be influenced by the fact that patients with coarctation tend to die young, and to die of their coarctation. In Maud Abbott's series 74 per cent died before or during their 40th year. This being so it is important to try to assess the added risk to life which may be entailed by the occurrence

of pregnancy in such a patient. It appears to depend mainly on two factors which are, firstly, the ability of the heart muscle to withstand the increased circulatory load of pregnancy and labour in addition to the stress of the congenital lesion, and secondly, the integrity or otherwise of the vascular system. Examination of the causes of death in Abbott's series indicates that these two considerations are of roughly equal importance in cases of coarctation in general. Of 200 cases, 155, 77 per cent, died as a direct result of the lesion, analysis showing that the immediate causes of death were:

Rupture of the aorta, 44; cerebral haemorrhage, 24; failing circulation, 60; sudden cardiac asystole, 17; bacterial endocarditis, 10.

Congestive failure was commoner in the older age groups, and vascular accidents in the younger patients, and it is reasonable to suppose that longstanding hypertension, together with minor infections, weakens the myocardium more after middle life than before. Consideration of the physiology of pregnancy serves to remind us that a notable increase in the circulatory burden falls upon the myocardium. According to Hamilton and Thomson[17] the major alteration in the circulation of normal pregnant women consists of an increase in total blood volume up to 45 per cent, starting early in pregnancy, becoming maximal about the 36th week, and decreasing gradually during the last 4 weeks (more rapidly in the puerperium until the non-pregnant level is reached 14 days after delivery). The placental site, acting as an arteriovenous aneurysm, is probably responsible to some extent for the blood volume changes, but the decrease in the blood volume which occurs before separation of the placenta, suggests a hormonal rather than a purely mechanical control. The increased work of the heart is accomplished by increasing the output per beat and the number of beats per minute. Strayhorn,[18] who reported a case of coarctation with observations on the cardiac output during and after pregnancy, concluded that the increase in cardiac output was of the same order as a normal pregnant woman may show, and clinical reports bear out the belief that patients with coarctation support the stress of the increased circulatory burden of pregnancy remarkably well. Few cases have been described as terminating in congestive cardiac failure during pregnancy or shortly after delivery. Fawcett's patient died in congestive cardiac failure 14 days after the birth of her 9th child. She was 45 years old, and suffered from bronchitis. The patients of Maxwell,[5] Laffont and Laffargue,[19] and Lian and Frumuson[20] showed signs of congestive failure early in pregnancy. Maxwell's patient, who failed at the 5th month of her 4th pregnancy, recovered with rest, but the final outcome was not stated. The other patients were treated by therapeutic abortion followed by sterilization. Abbott's patient was a primipara of 34 years, with mitral and aortic stenosis in addition to coarctation. She presented signs of cardiac insufficiency during pregnancy and was delivered by Caesarean section at the 8th month. She " died quietly in her sleep 6 nights later," but the precise cause of death is not stated. Bramwell and Longson[6] described a patient who developed auricular fibrillation, dyspnoea, oedema of the ankles and albuminuria in her 2nd pregnancy and was delivered of premature stillborn twins, but she was also severely anaemic and possibly had toxaemia of pregnancy. They observe that " coarctation of the aorta often seems to impose surprisingly little additional burden on the heart." Sudden death from acute heart failure in pregnancy has not been recorded, but Strassman, and Hamilton and Thom-

son both described one instance of this outcome many years after the patient's last pregnancy The latter authors, with an extensive experience of cardiac patients in pregnancy, and who themselves observed 4 cases of coarctation during pregnancy, gave a good prognosis, but advised that such patients be treated with a régime of restricted exercise, and carefully guarded against unnecessary strains. In only one case, however, was the patient delivered by Caesarean section.

Mendelson, on the other hand, takes a much more gloomy view, going so far as to advise against conception, and holding that induction of abortion with sterilization is indicated if the patient is seen in early pregnancy. He found reports in the literature of 5 patients who died during pregnancy or shortly after delivery, and of 10 patients who suffered exacerbation of their symptoms during pregnancy. Of the former 3 died from rupture of the aorta (these were the patients reported by Strassman, Katz and Leudet), 1 from cerebral haemorrhage at the 9th month (Kreigh) and 1 from cardiac failure (Fawcett's patient, already referred to). Of his own 3 cases 1 was stated to be less well 10 weeks after delivery than she was before pregnancy, and 1 was apparently normal. The The third was undelivered at the time of the report. He intended that she should have a Caesarean section because of the possibility of a vascular accident, the frequency of which he very rightly stressed. Many authors have noted the association of congenital anomalies such as pathological thinning of the aorta and bicuspid aortic valve with coarctation. Harrison[21] described cystic medial degeneration of the ascending aorta with associated dilatation proximal to the coarctation in a man who, however, died not of rupture of the aorta but of cardiac failure. Kinney et al. reported a case of coarctation and dis-

secting aneurysm of the aorta in a 23-year-old woman who was 6½ months pregnant. Postmortem examination showed changes in the aorta similar to the medial degeneration described by Harrison and others. Maud Abbott, as before mentioned, also emphasized the frequency with which cases of coarctation of the aorta terminate in rupture of the aorta or cerebral haemorrhage. Billinghurst described a patient who was free of symptoms during pregnancy until the onset of labour, when she fainted. Recovery was rapid and appeared to be complete, the baby being born without obstetric intervention. Twelve hours later, however, the mother died suddenly, and a postmortem examination revealed rupture of the aorta as the cause of death, with evidence to suggest that the aortic dissection had started some hours before death, presumably when the patient fainted.

Acute failure of the left ventricle during pregnancy or labour might be expected, but in fact appears to be uncommon. Strassman reported a patient with coarctation who had had 7 children, and who died suddenly at the age of 56 years, apparently of acute heart failure. Walker's patient, a primigravida of 31 years, with arm blood-pressure 210/100, left ventricular hypertrophy and poor exercise tolerance, developed acute dyspnoea and distress in the second stage of labour but was successfully delivered by forceps and had an uneventful puerperium. The author concluded that labour should be avoided and Caesarean section performed at term, a view with which many authors concur, particularly Mendelson.

Subacute bacterial endocarditis complicating coarctation might possibly be initiated by sepsis introduced during labour, but a search of the literature does not reveal any obvious relationship except Dustin's[22] patient who died 6 months after delivery. She was a primipara of 17½

years with classical signs of coarctation, who complained only of slight dyspnoea during pregnancy. She had a normal delivery. Symptoms attributable to sub-acute bacterial endocarditis commenced about 2 months afterwards and she died of proven endocarditis. Mendelson's summary of the literature also uncovered 1 case of death from subacute bacterial endocarditis, but symptoms did not begin until 6 months after delivery.

The hypertension which complicates coarctation, being a vascular surcharge of the upper part of the body only, does not appear to carry with it any increased danger of pre-eclampsia, which, if it occurred, would be of very grave import to a patient with coarctation. Hypertensive encephalopathy is described by Hamilton and Thomson in 1 of the 4 patients personally observed by them. Convulsive attacks with loss of consciousness occurred during the 8th month of pregnancy, but the patient was delivered normally. She died suddenly 7 years later, no other pregnancies having occurred, but the cause of death was not determined.

We contemplated these hazards while supervising the pregnancy of another patient.

Mrs. R. S., gravida 1, aged 26 years, was first seen July 30th, 1945, when 3 months pregnant. She gave a history of two attacks of rheumatic fever at 7 and 14 years of age, at which time her heart was thought to have been affected. However, she led a moderately active life and was free of symptoms except headaches. At 19 years of age she had an examination for life assurance and was found to have a high blood-pressure. In 1942, she joined the W.A.A.F. and led a busy but not physically strenuous life till 1944, when she began to complain of increasing fatigue, breathlessness and giddiness on exertion, and fainting attacks. Two years before, the patient had had an attack of breathlessness at night which ended with the

coughing of bloodstained, frothy sputum, and for which she was suspected to be tuberculous. During the last 2 years she had also had infrequent attacks of precordial pain brought on by exertion and attributed to indigestion (the patient's exercise tolerance appears to have been extremely variable). In 1944 she was investigated because of her complaints of headache, breathlessness and fainting, and was diagnosed as a case of coarctation of the aorta. She was invalided from the service and advised not to become pregnant.

When examined by us she was found to be well-nourished with a regular pulse, rate 84 per minute. Arm blood-pressure was 208/104 on the right side, 190/108 on the left. The blood-pressure was not obtained in the legs, and pulsation could not be felt in femoral or peripheral leg arteries. There was marked pulsation in the suprasternal notch and visible pulsation in both infrascapular regions. Large pulsating vessels could be felt along the medial scapular borders. The apex beat was diffuse and the heart did not appear to be enlarged clinically. There was a systolic murmur at the base, loudest in the third left intercostal space, and conducted upwards to both sides of the neck, being also well heard between the scapulae on the left, at the level of the fourth rib. No thrill was felt. X-ray of the chest showed moderate cardiac enlargement with hypertrophy of the left ventricle, absence of the normal aortic shadow and notching of the lower borders of the fourth and fifth ribs. The lung fields were clear. An E.C.G. showed left ventricular preponderance. Palpation of the abdomen disclosed an enlarged uterus of the size of 14 weeks' gestation. The liver and spleen were not enlarged, and abdominal aortic pulsations were not felt.

It was at first intended to terminate the pregnancy, but we felt that this was not justifiable without sterilization, which the patient was not prepared to accept. Further enquiry and examination of the literature caused us to modify this view, and as the patient promised to submit to a cardiac régime, it was decided that she should continue the pregnancy and be delivered by Caesarean section at term.

She restricted her activities to a minimum and did no housework, but only had one period of rest in bed, i.e. the 2 weeks under observation in hospital, initially. After this her symptoms of headache, breathlessness and giddiness on exertion, were slightly improved and further bed-rest appeared to be unnecessary until near term, when they again increased a little. The blood-pressure varied, but never rose higher than at the initial examination. After resting in bed it actually fell as low as 130/90 (right arm), the average being 190/100. Albumin was not found in the urine at any time during pregnancy, and from the obstetric point of view everything was normal.

She was readmitted at the 37th week of pregnancy for further rest before delivery. There was *no objective sign of decompensation but the blood-pressure remained high*. An elective low classical Caesarean section was performed 3 days before the expected date of delivery. Anaesthesia consisted of local injection of 1 per cent procaine using the rectus block method, with additional skin infiltration. Omnopon gr. ¼ was given intramuscularly at the beginning of the operation and, as soon as the baby was delivered, morphia gr. ⅙ was given intravenously. The abdominal wall was more vascular than usual, but the uterine loss was normal. Palpation of the abdominal aorta showed the vessel to be pulsating feebly and of about half normal size. The patient stood the operation well, and the baby, a 9 pounds 6 ounces female, was in excellent condition. The puerperium was uneventful and the patient was discharged 3 weeks after delivery, her cardiovascular system showing no change on examination. Attempts at establishing breast feeding were only partially successful, because the patient was not co-operative in this respect.

Six months later she stated that she was less breathless than before pregnancy. Her arm blood-pressures remained at the same level as before delivery and she still complained of headache. The size of the heart was unchanged clinically and radiologically, but the systolic murmur was now much less pronounced. An E.C.G. showed left ventricular preponderance of the same degree as before. The patient appeared to have been quite unaffected by the pregnancy but was given contraceptive advice. It is proposed to make a

reassessment of her cardiac condition in about 2 years time before considering another pregnancy.

We have permission from Dr. Paul Wood and Dr. Horace Evans to quote 2 further cases, as yet unpublished.

(1) Mrs. A. B., 5-para., now aged 37 years, with classical signs of coarctation of the aorta and slight cardiac enlargement, has had 5 normal deliveries and refuses sterilization.

(2) Mrs. S.Z., secundigravida, aged 31 years, was first seen when 3 months pregnant. She had had a normal delivery 18 months previously but had been told to rest during pregnancy because of a raised blood-pressure. On examination her arm blood-pressure was found to be 210/100 and leg pressure 120/100. A widespread systolic murmur was heard over the precordium and pulsations were felt in both scapular regions. Clinically and radiologically the heart appeared moderately enlarged and the aortic knuckle was small. She was rested in hospital for the last 3 months of pregnancy, and had a normal delivery and puerperium.

In spite of these reassuring results and other reported cases indicating the safety of vaginal delivery for patients with this anomaly, we still feel inclined to play for safety in view of the experiences of Walker and Billinghurst, favouring delivery by Caesarean section. It is clear, however, that pregnancy is not contra-indicated in the majority of these patients, though adequate spacing and avoidance of late childbearing seems a wise precaution.

SUMMARY.

The literature on coarctation of the aorta in association with pregnancy is reviewed. One new case is described in detail, and brief notes of 2 other cases not under our care are appended.

We would like to thank Dr. Evan Jones for seeing our case and encouraging us to

allow pregnancy to continue. Our thanks are also due to Dr. Horace Evans and Dr. Paul Wood, who have kindly allowed us to quote their cases, and to the large number of obstetricians and physicians who have been good enough to search their records in an endeavour to find other unreported cases.

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FIG. 1.

Testicle of E.B. (K.161).
Magnification × 150

H. & S.

A Case of Intersexuality—A Clinical and Hormonal Study

BY

A. M. HAIN,[*] D.Sc., and J. EWART SCHOFIELD, F.R.C.S.

IN the main, intersexuality can be classified into 2 types: the type in which there is a variable degree of malformation of the internal and external reproductive organs due to an embryological fault, and the type in which the secondary sex characters are made to resemble those of the opposite sex under the influence of the excessive hormone secretion of a gonadal tumour or of the adrenal cortex. One is tempted to call the first " genital" and the second " endocrine" but for the fact that instances of the " endocrine " type have been found in newborn infants and the " genital " type may have an endocrine basis.

The patient to be described belongs to the first class and can be more accurately described as a male pseudohermaphrodite, i.e. a person born with male gonads but only partial development of the corresponding external genitalia, and with certain female secondary characters present. The patient was brought up as a girl.

Description of case. When aged 2½ years E.B. had a testicle removed during an operation for right inguinal hernia. When 14 years old " she " consulted J. E. S. for hernia on the other side; the patient was quite unaware of any doubt as to her sex and a full examination could only be made under an anaesthetic.

General appearance. Five feet nine inches in height, generous growth of head hair (red), no axillary or pubic hair, some hair on forearms and on front of legs. General contour of male type: narrow pelvis, absence of female waist, flat breasts, inverted nipples; X-rays showed that the epiphyses were not closed.

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External genitalia. At first glance seemed definitely female; labiae present but not well marked. Clitoris size of red end of match; urethra was of female type; poorly developed hymen. Vagina would admit thumb, but ended abruptly and was only 1¼ inches long; no cervix.

Operation for inguinal hernia. Hernial sac was exposed along what looked like the round ligament and opened right up to internal ring in which testicle lay. What was at first thought to be round ligament was the gubernaculum which appeared to find insertion in the region of the pubic spine. By enlarging the opening of the neck of the sac, it was possible to pass a hand into the peritoneal cavity in order to ascertain what secondary sex structures were present. Uterus, Fallopian tubes and ovaries were completely absent. The testicle was removed.

Histologically, the general appearance of the excised testicle was that of a cryptorchid rather than one of adolescence. The few tubules present were lined with a single layer of germinal epithelium; there were large areas in which tubule-formation had disintegrated and in some place degeneration was so far advanced that only a tubular cells were interspersed with a background of connective tissue; quite a third of the testis was connective tissue. There was also a considerable amount of interstitial tissue, part of which appeared to be secretory (Fig. 1).

Hormonal findings. The patient's daily hormone output prior to operation was: 17-ketosteroids: 11.9 and 6.7 mg.; pregnanediol: none; combined oestrogen: <2 I.U.; gonadotrophin >106 M.U. The methods of hormone estimation used were: ketosteroids—Patterson's (described by Hain 1947); pregnanediol—Venning (1938); combined oestrogen—Callow *et al.* (1939); gonadotrophin—modification of Scott's (described by Hain, 1947).

As the average adult male and female excrete respectively 13.3 and 7.4 mg.

17-ketosteroids daily, the androgen excretion of our patient, taken in conjunction with an absence of pregnanediol excretion, ruled out the possibility of hyperplasia or tumour of the adrenal cortex being the underlying cause of the intersexual condition. Owing to the overlapping of hormone values for the 2 sexes it is not possible to determine sex by reference to the excretion of androgen and oestrogen. The absence of any detectable oestrogen excretion is not surprising as the patient had no more than a single rudimentary gonad.

The most interesting feature hormonally is the very high gonadotrophin output: >106 mouse-uterine units (M.U.). In a series of women and men Werner (1941; 1943) demonstrated that apart from peaks of excretion around ovulation in the former, and spurts of varying duration in the latter, the average gonadotrophin output for both sexes was between 5 and 20 M.U. per 24 hours. In women values might rise to 40–80 M.U. around ovulation; in men they rarely exceeded 40 M.U. Evans and Gorbman (1942) detected 6–20 M.U. gonadotrophin per litre in men. The explanation of the excessive secretion of gonadohin (follicle-stimulating hormone) lies in the fact that our patient was a cryptorchid. Martins (1930) noticed that, in animals, cryptorchidism led to histological changes in the anterior pituitary which, though less pronounced, resembled those following castration, including the presence of " castration cells ". This experiment and those of Nelson (1934a; 1934b) suggested that castration, and to a minor degree cryptorchidism, so affected the pituitary that it produced a continuous and enhanced supply of follicle-stimulating hormone and little or no luteinizing hormone; parabiotic union of a normal female with a cryptorchid male caused the female to be in constant oestrus accompanied by excessive follicular development of the ovaries without luteinization. The striking observation in our case is that a person aged only 14 years should have been excreting gonadotrophin in amounts typical for the adult castrate. The implication is that the pituitary is susceptible to gonadal influence for a considerable time before puberty is reached. It is commonly held that the anterior pituitary does not become active until puberty and, in the absence of a satisfactory method of recovering urinary gonadotrophin, none had been detected in the urine of children. Supporting this premise, Henderson and Rowlands (1938) found that the gonadotrophic potency of the human pituitary is slight during early childhood. In order to throw light on this point, the gonadotrophin excretion was ascertained (by A.M.H.) in a number of children of both sexes from 5 to 14 years of age. As in the adult, so also in children, there are considerable fluctuations in hormone output in the same individual. In 9 girls between the ages of 5 and 9 years the gonadotrophin output varied from <2 to 10 M.U. daily, and in 8 boys aged 8–12 years the range was <2–18 M.U. daily; a boy aged 14 excreted 14 and 28 M.U. Since it is thus obvious that the anterior pituitary secretes gonadotrophin from an early age, it is not surprising that cryptorchidism in a child should have the same effect on pituitary function as that produced in an adult.

A somewhat similar case was described by one of us (Hain, 1947) in which the child was only 8 years old. There was no other symptom of virilism than an hypertrophied clitoris; the ketosteroids were less than 2 mg. per 24 hours but the daily gonadotrophin output was 20 M.U. Quite rightly operation has been postponed until the patient is a little older as the surgical procedure in such cases is generally determined by the psychological outlook of the patient, whether dominantly male or

female. It is probable that Dr. T. N. MacGregor's patient (Hain, 1947) is another male pseudohermaphrodite but unfortunately permission to operate was not granted. In this case the patient was brought up as a girl until 17 years old, when, in addition to a penis and vagina, a testicle in each inguinal canal was found. As only a small sample of urine was received for analysis, it was not possible to estimate more than the 17-ketosteroids output, which was 15.6 mg. per litre of urine—a figure which does not denote any appreciable hyperfunction of the adrenal cortex.

One naturally tends to think that the urinary androgens are excreted by the testes but only a small proportion is derived from this source. This is shown by the fact that women excrete almost as much 17-ketosteroids as men, and that eunuchs excrete very little less than normal males. Their chief source is the adrenal cortex and in hyperplasia or tumour of the cortex the androgen excretion may run into hundreds of milligrammes per 24 hours.

This raises another interesting point. In cases of doubtful sex it is possible, with a knowledge of the 17-ketosteroids output, to differentiate between virilism in a female due to adrenal cortical hyperfunction (female pseudohermaphroditism) and faulty development in a male due to a lack of suppression of primitive female structures (male pseudohermaphroditism). In the female with pseudohermaphroditism the excretion of 17-ketosteroids is greatly in excess of the normal range and may even exceed 100 mg. per 24 hours: generally, though not invariably, pregnanediol also is excreted. Young (1937) cites 17 examples of the condition taken from the literature, to which he adds 4 of his own, in all of which the abnormality was associated with greatly enlarged adrenals. Typical cases have recently been described by one of us (Hain, 1947). On the other hand, the male

pseudohermaphrodite excretes normal amounts of androgen or values only slightly above normal, and Neugebauer (1908) found that in only 0.7 per cent of cases was there bilateral hyperplasia of the adrenal.

The defect in the male pseudohermaphrodite is attributed by Young to malfunction of the interstitial cells of the testis in the embryo. In his opinion a certain quality of the gonad is required to bring about full development of the external genitalia and, in male pseudohermaphrodites, the necessary stimulus was not at hand at this stage of embryological development and consequently the penis, prostate and seminal vesicles did not form. Young's suggestion implies that the gonad secretes before birth, which is very doubtful; indeed all the evidence admirably reviewed by Moore (1944) is strongly against such an idea. Broster and Vines (1933) attribute the abnormality to malfunction of the adrenal cortex at a critical stage of embryonic development. In the foetal adrenal, according to these authors, the cortex has a strong masculinizing influence from the 10th to the 18th week in the male, whereas a weaker influence is exerted in the female and only from the 11th to the 14th week. The "masculinizing influence" in our case was established early enough to suppress the ovaries and uterus but not the rudimentary vagina; it is feasible to suppose that the androgenic function of the adrenal cortex was too weak, however, to bring about full development of the male secondary characters. At the same time it is curious that there is almost complete suppression of the female secondary sex apparatus in association with such slight development of that of the male both internally and externally. In the 8 male pseudohermaphrodites described by Young the extent to which the development of the external genitalia was arrested and Mullerian structures were present was, on the

whole, in inverse ratio to the development of male structures. Departure from this general rule might be due to differences in tissue response or in the initial stimulus and the time of its impact, or again in some cases the explanation may lie in a disturbance of the chromosome formula. Evidence in favour of a hereditary basis for the condition has been put forward by Kallmann *et al.* (1944). In the opinion of Novak (1935) such patients are genetic females in whom the sex reversal took place at an early phase of development. On the other hand, statistical evidence strongly suggests that these were genetic males; the sex distribution in such families taken from the records of Bonnier and Moebius and quoted by Witschi (Allen, 1939) is as follows:

Sex distribution in families with hereditary male pseudohermaphroditism (m.p-h)

Sex of children.

♀	♂	m.p-h.
58	13	42

55

Witschi adds thereto 2 families exhibiting a hereditary type of hypospadias which is supposed to represent the lowest grade of pseudohermaphroditism and in which the sex distribution showed a similar tendency. In our case the only other member of the family was a brother.

In such cases the problem that faces the surgeon is one of procedure. Should the testis be left or removed? As a rule the patient is psychologically female and either this fact or the wishes of the parents determine for the surgeon what course to adopt. All the patients referred to below, including our own case, were female in disposition and the question was rather one of possible risk in retaining the gonad. Broster and Vines (1933) performed bilateral orchidectomy in their 2 cases (Nos. 17 and 18); Novak (1935) also removed the testicle in

order to be certain that male characteristics did not develop. Young (1937) on the other hand, replaced the testicle in the abdominal cavity in the belief that it might be the source of the oestrogen responsible for the feminine disposition of the patient. By retaining the testis there would, in our opinion, not only be the risk of its becoming secretory and giving rise to embarrassing symptoms of virilism, but also it might become the seat of a teratoma at a later date. In the case of E.B. very little oestrogen was recovered by urinary analysis and it is unlikely on this and on histological grounds that the gland removed was secreting effective amounts of this hormone. There was no doubt about the feminine disposition of our patient. She was observed while in hospital to be " very keen on her personal appearance, often combing her hair and busy with her face toilet . . . not at all unattractive . . . blushes easily."

SUMMARY.

A male pseudohermaphrodite, aged 14, is described.

It was possible by estimation of the excretion of 17-ketosteroids (urinary androgens) to distinguish between male and female pseudohermaphroditism and so to exclude adrenal cortical hyperfunction.

An excessive excretion of gonadotrophin (F.S.H.), typical of cryptorchidism, was an outstanding feature and demonstrated that the pituitary secretes, and is itself under gonadal influence, before puberty.

The probable origin of the developmental defect is discussed.

The question of the procedure to be adopted by the surgeon in such cases is debated.

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A Survey of Gynaecological Surgery

BY

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THE progress of gynaecological surgery for the last 40 years has been marked more by the modification of old operations than by the introduction of new ones. This is not to be wondered at seeing that our art was handed on to us by surgeons at least as ingenious and persistent as ourselves: "There were great men before Agammenon."

Of the really new operations I would place first McIndoe's grafting operation for the construction of a vagina. Its results are remarkable, the canal thus fashioned being, after a very short time, indistinguishable from the normal vagina. Best of all it carries practically no risk with it, and of the 46 operations which McIndoe has now performed in conjunction with various gynaecological surgeons every patient has recovered, and there was only one in which the desired end result was not accomplished. I have no doubt at all that it should replace all other methods of constructing a vagina. Of these Baldwin's operation is the best known but the transplantation of a segment of ileum entails a very definite risk to life. Such disasters do not get into the medical press, but I know of two, both women dying of intestinal obstruction at the site of the anastimosis. Such a happening is doubtless preventable but obviously there are other risks besides this one. I have performed the operation 7 times and am heartily glad that I shall never need to perform it again; for it is a most responsible procedure and one which puts a great strain on the surgeon. Moreover its risk limits its application to those cases where abolition of the deformity is urgently called for, whereas McIndoe's operation is so safe that it can be advised in any case, irrespective of whether the girl has marriage in prospect or not. What I have said about Baldwin's operation applies equally to the transplantation of a segment of the large bowel. Skin grafting operations to remedy the deformity in which the graft is whole-thickness skin are clumsy and tedious in performance, whereas McIndoe's operation can be carried out very quickly. It will, I think, always involve the co-operation of a plastic surgeon with a gynaecological surgeon since the latter has no opportunity of becoming expert in the cutting of a large superficial graft.

The second new operation I would mention is the suspension of the urethra by strips of abdominal fascia to rectify stress incontinence. This operation, which originally derived from the continent, has been well put to the proof by Chassar Moir (1945) in England and Aldridge (1944) in the United States, but in my opinion the best technique is that recently introduced by Terence Millin whereby the suspension is effected entirely through the abdomen, instead of the two-way approach previously employed. Excellent immediate results have been obtained

by all the surgeons named, but we must bear in mind that sufficient time has not yet elapsed to estimate the long-term results, for the tissues may stretch again. Even if such is proved not to occur I think that in the majority of cases of stress incontinence, the far lesser vaginal operation, which I originally devised 30 years ago, should be given a trial before resorting to the newer procedure which is of much greater magnitude.

It should be noted that neither of the two surgeons who have thus contributed to gynaecological surgery are themselves gynaecologists, and indeed all the great advances in this field stand to the credit of men who had other surgical interests besides gynaecology. Narrow specialism, though it achieves excellence in established procedures, seems to be unproductive of major progress.

The total hysterectomists continue to be vocal with, I think, harmful results, for while in expert hands the risk of removing the whole uterus is very little greater than removing the corpus only, in the hands of surgeons who only occasionally invade the pelvis is quite otherwise. I mind me of an unfortunate nullipara of 30, who, having a single fibroid, had her uterus and the base of her bladder removed together! All gynaecological surgeons of experience have come across such cases and genito-urinary surgeons are quite familiar with them. The threat of carcinoma in the retained cervix has always left me cold. In my series of 500 Wertheim operations there were 7 stump carcinomas and in 3 of them the growth was undoubtedly present when the subtotal hysterectomy was performed. It must be remembered, too, that cases of carcinoma of the cervix, as a class, have a much more stormy obstetrical and gynaecological history than the average woman, and amongst them the proportion of individuals who have undergone a previous operation is above the general average. The difference of opinion chiefly concerns hysterectomy for fibroids. Now a large proportion of these patients have never borne children and thereby have escaped the common determining cause of carcinoma of the cervix. An obviously unhealthy cervix, especially if split, should, of course be removed with the corpus but for the rest the least operation which effects a cure should be chosen.

Wertheim's operation continues to be carried out by a number of gynaecological surgeons despite the confident prophecies of the all-out advocates of irradiation, and it is interesting to note that in the United States, where for years the operation had been very little practised, there is a swing in favour of surgical measures. This is as it should be, for some cases of carcinoma of the cervix are better treated by surgery than by irradiation, and it would be an irreparable loss to gynaecology if the skill necessary to do the operation was permitted to die out.

Myomectomy has an increasing vogue amongst the elect but hysterectomy is still constantly being performed by the less skilled in cases where the conservative operation would be just as feasible and safe, or even safer. This is a matter for education in which the leaders of our calling must be the exemplars and teachers. The scope of the operation has been enormously enlarged, chiefly because means have been found to obstruct the blood flow to the uterus during the operation, and it can be claimed that, as far as the technical difficulties dependent on the number, size and position of the fibroids are concerned, the operation can be carried out on at least 95 per cent of the cases. This is a great advance, for the surgeon now has a free hand to decide whether conservative or radical measures best accord with the patients' interests, instead of being pressed

or driven to hysterectomy by fear of the difficulties and risks attaching to myomectomy.

Conservative surgery has been further enlarged by the operation of ovarian cystectomy, whereby ovarian cysts are shelled out and the whole of the ovarian substance conserved. The operation is applicable to all obviously innocent cysts and is specially beneficent to those cases where, in a young woman, both ovaries present multiple cysts—follicular, chocolate, or dermoid. Stanley Way (1946) has pointed out that in the case of ovarian cysts, recently and not severely twisted, if the surgeon, having untwisted the pedicle, will wait a little while, circulation re-establishes itself and ovarian cystectomy can safely be carried out instead of ovariotomy.

The operation appears to be a singularly safe one, there being no deaths in a series of over 300 operations recently reported. The importance of conserving all sound ovarian tissue is being increasingly recognized but the needless removal of ovaries is by no means extinct as yet.

Turning to the surgery of the Fallopian tubes, the reduction in the incidence of gonorrhoea and still more the improved methods of treating it, have greatly reduced the number of these cases, so common 40 years ago, where a double pyosalpinx with ovarian abscesses, and extensive adhesions made the necessary operation a very severe and difficult one. In my younger days two or three of such cases could be found in any gynaecological ward on any day of the year.

The conservative surgery of the Fallopian tubes (salpingostomy, tubal re-implantation) logically followed the introduction of tubal insufflation, and various operators have published their results. These are frankly disappointing, only 15 to 18 per cent of the patients wishing to have a child having become pregnant afterwards; and some surgeons have become disheartened and hesitate to advise an attempt to reopen closed Fallopian tubes. I deprecate this defeatist attitude. That success can be obtained is clear, and if, as I believe, imperfect technique is the cause of its rarity, our course surely is to improve upon it and not abandon the operation altogether. It has been stated that operatively reopened Fallopian tubes almost invariably become closed again within a year, but I know of many cases which contradict this pessimistic view.

For retroversion, shortening of the round ligaments by one or other of the many methods holds the field and the older ventral fixation is not often performed nowadays. The disrepute into which it has fallen derives from a distinguished gynaecological surgeon, who took to fixing the posterior wall of the uterus and when disasters in pregnancy began to accumulate denounced the whole operation, however performed! His voice was so authoritative that textbook after textbook down to the present day has repeated the condemnation. As a fact, fixation of the anterior wall has absolutely no effect on pregnancy or labour, and there are times when it should be chosen instead of round ligament shortening.

Long experience has taught me that there is one definite disadvantage to ventral-fixation, it is this: the posterior pelvis is abnormally opened up, with the result that a larger proportion of intestine occupies it. This increases the intra-abdominal pressure in Douglas's pouch, and if the posterior vaginal vault is already weak a prolapse in that situation (hernia of Douglas's pouch) is liable to develop. I have knowledge of 4 such cases in the last 10 years.

The reparative operations for prolapse have become pretty well standardized and

are so successful that pessaries are now only rarely advised. The vogue for removing the uterus as part of the operation is fashionable on the other side of the Atlantic and has some followers in this country: I hold it an entirely unnecessary thing to do (unless, of course, the uterus needs removing for a cause additional to the prolapse) and a relic of the old false view embodied in the lay expression " falling of the womb." Prolapse is the result of the vagina partially or completely turning inside out, and as such it is a purely vaginal phenomenon. The uterus by its bulk obstructs the movement, which is why complete prolapse is scarcely ever seen except in women past the change of life, or in those on whom total hysterectomy has been performed. The most difficult cases of complete prolapse to cure by operation are those where the patient has previously had her entire uterus removed. What I have said does not imply that the operations which include hysterectomy fail to cure the prolapse: they do; but the same result can be achieved without this needless enlargement of the operation.

As regards those disappointing cases where, after a reparative operation has been performed, the patient some years later returns again complaining that " something falls "; I would point out that in a number of these instances the return to the surgeon is occasioned, not by the work he did having given way, but by the development of a prolapse in a new situation. Thus after posterior colporrhaphy a posterior vault prolapse or a cystocele may appear, or, after anterior colporrhaphy, prolapse of the anterior vaginal vault.

The marked improvement in the results of gynaecological surgery which has been brought about in the last 40 years is due not only to advances in the technical details of the operations and the introduction of new procedures, but equally to the great increase in the adjuncts to surgery which the surgeon of today now enjoys. Chief amongst these is the perfection to which blood-transfusion has attained. In my younger days the most severe operations (Wertheim's for instance) had to be performed without this powerful aid. Saline infusion was employed, but only when the patient was in extremis. In connexion with infusion I would call attention to the excellent work of Avory and Naunton Morgan who showed that ordinary saline solution puts a great deal too much salt into the patient.

Spinal and intravenous anaesthesia have contributed to the improvement in no small degree, while better theatre technique and more efficient methods of antisepsis have played a great part too. From 90 per cent of women S. Aureus, often haemolytic, can be recovered from the abdominal skin; a fact which should give all abdominal surgeons cause to think furiously.

The attention now being given to the prevention of air infection has great historical interest, for it revives the original Listerian teaching. Lister endeavoured to counter it by the carbolic spray and failed, whereupon a school of thought arose which maintained that the danger was non-existent; a perfect example of Huxley's dictum: that many a truth has been turned down because of the faulty argument with which it was propounded. The splendid work of Leonard Colebrook (1944, 1946) should be studied by all surgeons. He makes it perfectly clear that patients should come into the theatre covered only by a paraffined blanket, the clothing having been taken off outside; and that in the future every operating theatre should be air-conditioned and fitted with an air-filtering device.

The steady advance of our art, which I have tried to outline in this cursory review,

shows at least that there is no finality in surgery. In climbing the tree of knowledge we stand upon our predecessors' shoulders and pluck fruit which they could not reach and our successors will stand on our shoulders and reach further still. The thought is humbling, but salutory, for it forbids any of us to cease climbing when so much is ahead.

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BOOK REVIEWS

"Food and Nutrition." By E. W. H. CRUICK-SHANK, M.D. (Aberd.), D.Sc. (Lond.), Ph.D. (Cantab.), M.R.C.P. Regius Professor of Physiology in the University of Aberdeen. Edinburgh: E. & S. Livingstone Ltd., 16 & 17 Teviot Place. 1946. Price 16s. net.

THE author modestly describes his work as "a brief survey of the present knowledge of the Physiology of Food and Nutrition, and of the means whereby this country met the problems of feeding the nation during the six years of war." The survey is comprehensive and explores every aspect of the subject of nutrition from the prehistoric past up to the Food and Agricultural World Organization of to-morrow.

The book admirably fulfils its purpose as a guide for the use of medical students and practitioners, and for all who are concerned with the part food plays in promoting the welfare of the individual and of nations.

Professor Cruickshank is convinced that malnutrition normally exists throughout the world. In this country in 1938 roughly 30 per cent of the population were undernourished or wrongly nourished. In India, from Dr. Aykroyd's survey, a large proportion of the 400,000,000 inhabitants have a diet which never approaches the physiological requirements; the relationship between diet and the incidence of disease is plainly manifest in India.

It is many years since Sir John Boyd Orr, by statistical investigations in the United Kingdom, demonstrated that the food value of the family diet is, in general, dependent on the income. In the higher wage groups more was spent on milk, meat and protective foods. To distribute food to the best advantage the Ministry of Food gave priority to children, and mothers and invalids. Milk and meals are provided in schools and vitamin supplements made available free or at a low cost. Unfortunately these privileges are often not used by the mothers; the Scottish mothers, in this respect, have proved no more canny than the British housewives.

The physiological section of the book begins as is usual with an account of the energy requirements for each sex and as modified by age and activity. An outstanding feature is the graphic description of apparatus for estimating the basal metabolic rate and of the apparatus for estimating the energy value of foodstuffs. Famine in so many parts of the world has demonstrated with painful clarity that a supply of energy is the primary nutritional need. Later chapters give a clear account of requirements for protein, mineral salts and vitamins.

The application of this knowledge on a world scale is to be the task of the Food and Agricultural Organization. The agriculture of all nations is to be contrived on an interlocking design to avoid excesses and shortages in the supply of essential foods. Foodstuffs produced in physiologically planned proportions are, if anything ever goes according to plan, to be distributed equitably between the nations. It is easier to grow an

ample supply of cereals than it is of fats, protein, minerals and vitamins.

Education of the people is needed to induce them to eat a more wholesome diet. The rationing during the war has produced a better average level of nutrition followed by an improvement in the health of the nation. This gain will be lost if on release from constraint there is a reversion to white bread and sugar as staple energy foods. The wartime flour of 85 per cent extraction is approved by food scientists and, as Professor Cruickshank asserts, there is no reason to believe that the phytic acid in cereals exerts any rachitogenic effect in good diets. Correlated with this point it is wise, he says, to note that administration of excess of calcium, without a supply of vitamin D is likely to do more harm than good. It is important that each locality should review its iodine situation.

The value of the book is reinforced by the inclusion of numerical tables, statistical figures, diagrams and graphic illustrations of human beings and animals who have eaten neither wisely nor well. The index apparently has suffered from paper rationing and is austerely brief.

" Child and Adolescent Life in Health and Disease: A Study in Social Paediatrics." By W. S. CRAIG, B.Sc. (Glas.), M.D. (Edin.), F.R.C.P.E., F.R.S.E. Formerly First Assistant in the Department of Child Life and Health, University of Edinburgh, etc. With a Foreword by Professor CHARLES McNEIL, M.A., M.D., F.R.C.P., F.R.C.P.E., F.R.S.E. 1946. Price 25s. Edinburgh: E. and S. Livingstone.

The close liaison that is becoming increasingly established between obstetrics and paediatrics, and the present planning of both future services, will assure this book a warm welcome. Professor Craig has provided the historical background that is essential to the understanding of their past development in so far as child health is concerned, and gives an excellent review of the child health services as they are designed to-day. A useful section is devoted to legislation relating to child and adolescent welfare, and appendices list representative hospitals, special schools, societies, etc., concerned with children. The author is obviously aware that the " jigsaw " of child care is unfinished, but even so the difference between the Curtis Report on the care of children and the impression gained from Professor Craig's book is illuminating. The former makes clear that many of the admirable legislative and other provisions for children are liable to break down in practice, and lead to such tragedies as were revealed by the recent O'Neill case, whilst Professor Craig is perhaps rather more concerned with the progress that has been made since the Nineteenth Century and inclined to take a rosier view of the services as they exist to-day. He is also unusually tolerant of the legislative slow motion that until recently has ensured that reforms were only initiated when the case for them was abundantly proven. At a time when it is fashionable to belittle the achievements of the social services, it is salutory to have this illustration of how much has, in fact, been done for child health, both before 1939 and during the war years, and to see present conditions in perspective with those existing in the Eighteenth and Nineteenth Centuries. As a book of reference this will be found invaluable. It is copiously, if a little uncritically illustrated, and is admirably produced.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

Examination for the D.Obst. R.C.O.G., October, 1946

The following Candidates have been successful in the Examination for the Diploma in Obstetrics:

Tariq Munir Abbas.
John Schonberg Astbury.
Robert Henry Obuabasa Bannerman.
Alan Barker.
Arnold Priestley Bates.
Trevor Cory Beard.
Alan Victor Greenwood Bibby.
John Montgomery Bowen.
Samuel Burke.
Denis John Burnett.
Diana Butler.
Peter Haig Cardew.
Thomas Ernest Ashdown Carr.
Betty Josephine Clymo.
Christopher Kersley Cole.
Norman Keith Crooke.
Thomas Kenneth Davies.
Ruth Millicent Dearing.
Janet Margaret Done.
Kathleen Agnes Dru Drury.
Richard Christopher Dwyer.
Charles Thomas Fawsit Ealand.
William Stewart Rolleston Fenton.
Hugh Flack.
Mary Francis.
William Kingswell Frewen.
Kamel Girgis.
Mary Elizabeth Goodson.
Alfred Henry Grenz.
Geoffrey Edward Roper Hamilton.
Emily Gertrude Hamlyn.
John Robinson Hassan.
Lore Marguerite Hasslacher-Traub.
Joseph John Hayward.
Mary Angell Hewett.
Monica Margaret Hogben.
Frank Lionel Edward Hugh-Musgrove.
Eric Douglas Hull.
George Arnold Humphreys.
James Barclay Joyce.
Christine Kirby.
Thomas Henry Lawton.
Constance Gertrude Lee.
Joan Mary Levett.
Kathleen Vernell Lodge.

Ernst Lucas Loewenthal.
Alison Jean McNairn.
Kathleen Margaret Agnete Millard.
Vishwanath Vaman Mohile.
John Anthony O'Neill Mulcahy.
Nestor John Stanley Nathan.
Arthur Denness Newsholme.
Rosalind Mary Louisa Nicol.
John Michael Norman.
Richard Tonkin Norman.
Rachel Jacob.
William Bernard O'Brien.
James Joseph O'Donoghue.
John Joseph Francis O'Sullivan.
William Henry Phillipps.
Geoffrey Turner Pitts.
George Ernest Prendiville.
Robert Williamson Kinross Purser.
Jean Finlay Ramsay.
Mary Jean Reading.
John Stuart Redfern.
Theodore Francis Redman.
Brian Charles Middleton Reed.
Edward Ridehalgh.
Frank Leonard Robertshaw.
Thomas Wilson Roddie.
John Vincent Rose.
Helen Margaret Russell.
Henry Ernest Rutherford.
Llewellyn Charles Rutter.
John Archibald Sadler.
John Cyril Tabor Sanctuary.
Eleanor Margaret Sawdon.
Kenneth Bryan Scott.
Harold Needham Skelton.
Margaret Eleanor Anne Slater.
Sydney Alexander Swanson.
John Mervyn Thomas.
Richard Radford Trussell.
Charles Michael Ferrier Walters.
Philip de Silva Wijesekera.
Donald Mervyn Wilkins.
John Wills.
Benjamin Walter Wood.
Maurice Roy Woods.

REVIEW OF CURRENT LITERATURE

This review is made in collaboration with the Abstracts Service
of the *British Medical Journal*.

INDEX

ANATOMY

1. Superiority of the South African Negro or Bantu as a Parturient.

By O. S. HEYNS. *J. Obstet. Gynaec.*, 53, 405–429, October 1946.

2. Outlet Pelvimetry. A Commentary, and the Presentation of a Pelvimeter for Measuring the " Symphysis and Sacral Biparietal Distance ".

By H. THOMS. *Surg., Gynec. Obstet.*, 83, 399–402, September 1946. 9 figs., 4 refs.

3. The Muscle of Micturition. Its Rôle in the Sphincter Mechanism with Reference to Incontinence in the Female.

By W. T. KENNEDY. *Amer. J. Obstet. Gynec.*, 52, 206–217, August 1946. 12 figs.

If progress is to be made in the treatment of diseases of the female urethra, further study of its anatomy and physiology is required. The sphincter and muscles of the urethra, both smooth and striated, are variously described by different authors, so that it is certain that the anatomy of the part is not clear. To gain information on this subject a study of serial sections of the urethra has been made in two planes at right angles, which has given information regarding its musculature. Several photomicrographs are shown. As a result of these studies it is found that the levator ani muscle is inserted in the lateral part of the urethra at the junction of the middle and upper thirds. The true sphincter is composed of the circular smooth muscle surrounding the middle and upper thirds of the urethra, together with longitudinal smooth muscle; it may be regarded as a cylindrical sphincter. The intrinsic voluntary muscle fibres make up a single muscle of unusual shape and function which has been named the muscle of *micturition*. This muscle has two origins and two insertions and its own nerve supply from the pudendal trunk, and is independent of the other muscles *in the neighbourhood*. The origin is by two slips of muscle attached to the periosteum of the anterior medial face of the ramus of the pubis, and the muscle passes in the form of a purse string between the circular and longitudinal muscles of the sphincter to end in two slips which fuse with the longitudinal muscle in the bladder neck. This muscle is quite separate from the levator ani, the bulbocavernosus, ischiocavernosus, and the transverse perineal muscles. When the muscle of micturition relaxes, the true or cylindrical sphincter exhibits its maximum control and no'urine runs out of the bladder. When it contracts completely the cylindrical sphincter is distorted into an oval formation throughout its length. In this voiding state all urine can escape from the bladder. If complete contraction becomes permanent, complete incontinence exists. Any partial contraction will carry with it a corresponding degree of incontinence.

L. W. Lauste

PHYSIOLOGY

4. Studies Concerning the Cause and Purpose of Menstruation.

By O. W. SMITH and G. VAN S. SMITH. *J. clin. Endocrinol.*, 6, 483–492, July 1946. 1 fig., 30 refs.

5. Basal Temperatures in the Normal and Pathological Menstrual Cycle. (La temperatura de base en el ciclo menstrual normal y patológico.)

By A. FOIX. *Rev. méd.-quir. Pat. fem.*, 25, 133–157, May 1946. 14 figs., 32 refs.

Basal body temperature is ascertained by rectal temperatures taken each morning before rising. Precautions needed to obtain accurate readings include using the same thermometer for the same number of minutes at the same hour each day. Rectal temperatures are the most reliable, though some authors take temperatures by mouth. No food or drink must be taken before recording. Any slight febrile illness alters the curve and a characteristic curve is found in cases of pelvic infection.

In the normal menstrual cycle the basal temperature curve is bi-phasic—a phase of low temperature followed by one of slightly higher temperature. The change in the curve from lower phase to higher takes place in the normally menstruating woman 14 days before the onset of the next expected period, and this indicates that ovulation precedes the next menstruation by 14 days, no matter what the length of the cycle. It has been shown that oestrogenic hormones and testosterone cause a fall in temperature, while progesterone causes a rise. Other workers have shown that glycogen appears in the endometrium, indicating a corpus luteum phase, with typical changes in the endometrium, following the rise in basal temperature. They conclude that the normal change in temperature indicates ovulation. In metropathia the low basal level is maintained throughout the cycle.

Basal body temperatures may be used in various

ways: to study ovarian function, to determine the time of maximum and of minimum fertility, as a test of pregnancy, to determine the effect of treatment designed to promote ovulation, to guide biopsies done for evidence of the secretory phase, to investigate types of metropathia haemorrhagica, to study the aetiology and pathology of amenorrhoea, and to study the intermenstrual crisis and dysmenorrhoea. The author presents several graphs of basal body temperature in cases of pelvic infection, and shows that in such cases a higher curve is superimposed on the curve of the normal menstrual cycle, the height of the curve depending on the severity of the infection.

[This paper contains little that is original and is mainly a review of work by earlier authors. The chief interest lies in the observations on curves in cases of pelvic infection.]

Josephine Barnes

6. **Colorimetric and Biological Determination of Folliculin during the Menstrual Cycle and Pregnancy.** (Détermination colorimétrique et biologique de la folliculine au cours du cycle menstruel et de la grossesse.) By M. F. JAYLE, O. CREPY, S. VANDEL, and O. JUDAS. *Bull. Soc. Chim. biol.*, 28, 363–371, April–June 1946. 4 figs., 3 refs.

Determinations were made of folliculin (oestrone) by both chemical and biological methods during the menstrual cycle and during pregnancy. The chemical method had been described previously, and depended upon preliminary ethereal extraction of the phenolic fractions (from human urine), and subsequent purification and determination photo-colorimetrically. The chromogenic value was expressed in terms of oestrone, except where a strong phenolic fraction was separated and expressed as oestriol. By this method oestriol and a-oestradiol gave colour values respectively 1.7 and 2.2 times weaker than with oestrone. The biological assay was determined in ovariectomized rats and mice by examination of the vaginal smears according to the test described by Allen and Doisy. In this test a-oestradiol is 3 to 5 times more active than oestrone.

It was found that during the course of 7 normal menstrual cycles the colorimetric method gave values which were about 20 times greater than those obtained by the biological method. The initial level by the latter method was about 25 international units per day (0.1 μg. oestrone = 1.0

I.U.) rising to 160 I.U. at 21 days, then falling to the initial level by the beginning of the second cycle. The curve obtained by the colorimetric method showed 3 peaks, the most important of which was considered to be in the middle of the cycle at the time of maximum development of the corpus luteum. The results were interpreted on the assumption that the chemical method estimated the total chromogenic value of the phenolic steroid compounds, irrespective of their oestrogenic activity. The curve was thought to follow the physiological activity of the ovarian cycle, though at a different level from that found with regard to the biological assay of the oestrogenic activity in the urine.

The oestrogenic activity of the urine does not increase immediately following pregnancy; an increase in folliculin does not occur until about the second month when (in the biological test) there is a rise from 400 I.U. to 2,400 I.U. at 75 days. Only 2 pregnancies were observed (both in the same woman), 1 of which ended in a miscarriage at the fiftieth day, the other going to full term. At the beginning of the third month the chromogenic value of the urine (chemical test) increases from 600 to 1,300 μg. at 270 days. By separation of different phenolic fractions it was deduced that the increase of a-oestradiol during labour and at the termination of the pregnancy accounts for only a part of the oestrogenic changes which take place in the urine. It was thought that during the ninth month another unidentified oestrogen may be present.

R. Wien

7. **Colorimetric Estimation of Pregnandiol glycuronide during the Menstrual Cycle and Pregnancy.** (Dosage colorimétrique du prégnandiol glycuronide au cours du cycle menstruel et de la grossesse.) By M. F. JAYLE and O. LIBERT. *Bull. Soc. Chim. biol.*, 28, 372–381, April–June, 1946. 4 figs., 1 ref.

Pregnandiol glycuronide in urine was determined colorimetrically by a method involving 3 different types of estimation. The urine was first extracted with butyl alcohol at pH 10 and then washed with sodium hydroxide. It was then divided into 3 factions. (a) This was used during the normal luteal phase and at the beginning of pregnancy—the fraction was taken up in methyl alcohol and Tollens' colour reaction applied. The results were expressed in mg. of pregnandiol per 24 hours, and

gave an estimate of the total non-phenolic steroid glycuronides. (b) This estimation was carried out as described in the previous article after acetone precipitation. (c) This fraction was precipitated with ether, the estimation being based on the fact that the steroid glycuronidates are insoluble in ether, but soluble in methyl alcohol. Comparative estimations of creatinine were also performed. The results of estimation (a) and (c) were more reliable than those obtained by method (b), since this last method gave large errors during the final months of pregnancy.

Nine menstrual cycles were studied in one woman, and it was found that the pregnandiol glycuronide level increased from about 4 mg. at the beginning of the cycle to about 14 mg. at the end. During pregnancy the level increased sharply after 10 days (from the cessation of the last menstrual period) from about 5 mg. to 25 mg. at 30 days, at which level it remained until 50 days. It was concluded that the corpus luteum has a detectable increase of activity as early as the first 10 days of pregnancy, and that the chemical method of estimation employed afforded a good means of diagnosis in early pregnancy

                                                R. Wien

8. A Test for Determining the Time of Ovulation and Conception in Women.

By E. J. FARRIS. *Amer. J. Obstet. Gynec.*, 52, 14–27, July 1946. 1 fig., 30 refs.

The occurrence of ovulation is detected by the reaction of the ovary of the immature white rat to the urine of the patient. If ovulation is taking place the ovary becomes hyperaemic. A single tested strain of animals must be employed. Two ml. of urine passed on rising is injected subcutaneously into each of 2 animals. The rats are killed at the end of two hours and the ovaries removed, inspected, and the degree of redness compared with the colours of a Munsell colour chart. Reactions are classified as normal or abnormal, a normal reaction consisting of a deepening in colour of the rat ovary, on 3 or 4 consecutive days near the middle of the menstrual cycle. Reactions occurred earlier in shorter menstrual cycles. A number of patients experiencing normal reactions became pregnant, but none with abnormal reactions did so. Pregnancy occurred when coitus took place on the third or fourth day of colour reaction, but not when it was delayed until the reaction had disappeared. Urine assays showed that gonadotrophin was present at the time when the reaction was positive, thus correlating the observations with those of other authors who had shown a peak of gonadotrophin excretion at the time of ovulation. The 2-hour rat test is very sensitive to small amounts of gonadotrophin in the urine.

It is concluded that hyperaemia of the rat ovary in response to injection of urine from a woman in the mid-phase of the menstrual cycle is strong, though not conclusive, evidence that ovulation is occurring. The observation was checked by laparotomy in 1 case. The test is likely to prove of value in cases of sterility to determine the optimum time for coitus or artificial insemination. The third or fourth day of the colour reaction is the date on which insemination is likely to be successful. Technical details are important for success. The animals must be of a single tested strain and should conform to special limits for age and size. There should be standard lighting conditions for reading results.

                                         Josephine Barnes

9. Effect of Mucus Volume on Conception.

By G. RAPS. *J. Amer. vet. med. Assoc.*, 109, 275–276, October 1946. 7 refs.

Artificial insemination of cows is performed either by instillation deep into the cervical canal or by deposition of the semen just inside the os uteri; the latter is known as the " cervical splatter technique ". Veterinary surgeons are divided as to the relative merits of the 2 methods. It has been argued against the second method that in cows with a large amount of oestral mucus secretion the semen would be carried out before impregnation occurred. An investigation was undertaken to see how far this theoretical objection was valid in practice. Cows vary greatly in the amount of the flow. They were classified as having little or none, a moderate amount, or a copious discharge. In over 2,000 inseminations the proportion of pregnancies resulting in the 3 groups was almost identical (46 to 49 per cent in each group). The author concludes that the amount of mucus has no effect on conception.

                                            H. J. Croot

10. The Receptivity of Cervical Mucus to Spermatozoa.

By M. BARTON and B. P. WIESNER. *Brit. med. J.*, 2, 606–610, October 26, 1946. 3 figs., 13 refs.

The post-coital (Sims) test often shows, in cases of infertility, that the spermatozoa do not penetrate the cervical canal or, having penetrated, do not survive therein. This may be due to seminal deficiency or to abnormal cervical conditions, or to both. Cervical faults are not always apparent, and it is no longer possible to assume that the cervical mucus is receptive unless the post-coital test is positive. Semen and cervical mucus are virtually immiscible, and an interface is formed between them when they are in contact. Passage through the interface depends on the motility and penetrating power of the spermatozoa.

A simple test has been devised by which the process can be studied individually in special contact preparations, the receptivity of the cervical mucus being studied against fecund semen. Semen may also be assayed against normal cervical mucus obtained during the ovulatory phase. The technique of the method is described. It consists in making, on a glass slide, a capillary chamber charged first with cervical mucus and then with semen. The preparation is then examined under the microscope. A quantitative test may be made by using a circle 3 mm. in diameter drawn on the cover-slip, and counting the number of sperms entering and leaving the mucus per minute. Examination of normal specimens demonstrates the mechanism by which spermatozoa generally penetrate and survive in the cervical mucus. It is shown that mucus attracts sperms, and these congregate at the interface. A decrease in sperm density is seen with distance from the interface. Sperms survive 12 to 48 hours at room temperature in slide preparations, not 4 to 5 days, as they do in the living cervix.

In abnormal cervical mucus, the interface is formed, but 6 fairly definite types of deviations from normal are noted. In some, sperms pass the interface, but after a time they lose motility. In others, sperms do not pass the interface, but congregate there. In certain other cases there is a deficiency of cervical mucus. Cervical mucus must thus, if fertility is to be assured, allow motility of sperms, sustain sperm life, and be susceptible to invasion. Faults in the cervical mucus are commonly a cause

of infertility, and these results are closely correlated with those of the post-coital test. Infection, either general or local, or oestrogenic deficiency, may lead to abnormal cervical secretion. In cases of cervical infection the classical signs may be absent. Treatment has been attempted along 2 lines, by administration of oestrogens, either locally in the form of pessaries or by injection, and by the administration of sulphonamides in relatively small doses, sulphadiazine having been found to be the preparation of choice. An invasion test should be done in conjunction with routine semen analysis as part of the investigation of all sterility cases. [This is clearly work of great importance in the field of sterility.]

Josephine Barnes

11. Hydrogen Ion Concentration of the Senile Vaginal Mucosa Before and After Estrogenic Therapy.

By K. J. KARNAKY. *Sth. med. J.*, 39, 906–907, November 1946. 1 ref.

PREGNANCY

NORMAL
Physiology

12. The Relationship of Maternal Weight Gain to the Weight of the Newborn Infant.

By J. KLEIN. *Amer. J. Obstet. Gynec.*, 52, 574–580, October 1946. 12 refs.

13. Estimation of Urinary Oestrone in Pregnancy. (Le dosage de l'oestrone urinaire au cours de la grossesse.)

By C. MAYER. *Brux. méd.*, 26, 1181–1189, October 6, 1946. 3 figs., 28 refs.

The biological and colorimetric methods for the estimation of urinary oestrogens are described and their limitations discussed. It is generally agreed that in pregnancy there is a considerable increase in urinary oestrogens, which appears to depend on the secretory activity of the placenta. A new method of extraction of urinary oestrone is described. A 24-hour specimen is collected and a certain volume is hydrolysed with hydrochloric acid to liberate oestrone. Sodium benzoate is added. This causes benzoic acid, which acts as an adsorbent, to be precipitated. After filtration and washing in distilled water the precipitate is dried, dissolved in ether, and the ethereal solution is added to 20 per cent caustic soda. This removes the benzoic acid, which is reconverted into sodium benzoate. The ethereal layer is separated and

H

evaporated leaving an oily residue containing all the oestrone. The latter is then estimated colorimetrically.

The level of urinary oestrone was measured in 10 cases of pregnancy, 7 of which were followed until after delivery. It was confirmed that there is a considerable rise in urinary oestrone during pregnancy. In non-pregnant women the highest level recorded was 120 μg. (1μg = 10 international units). In 2 cases investigated at the sixth week of pregnancy, levels of 240 and 280 μg. were found. There is a gradual rise until at term levels of 2,400–4,200 μg. are found. There is considerable individual variation. One case of abortion at 4½ months is described. This case showed a much lower level of urinary oestrone than the rest at corresponding stages. This suggests that the placenta is responsible for the secretion of oestrone. Other evidence in favour of this is the sharp fall in urinary oestrone following parturition, and the general rough correlation between size of placenta and level of urinary oestrone.

R. Barer

14. **Permeability of the Placenta of the Guinea Pig to Inorganic Phosphate and its Relation to Foetal Growth.**
By W. S. WILDE, D. B. COWIE and D. B. FLEXNER. *Amer. J. Physiol.*, 147, 360–369, October 1946. 4 figs., 11 refs.

15. **Permeability of the Human Placenta to Isoantibodies.**
By A. S. WIENER and E. B. SONN. *J. Lab. clin. Med.*, 31, 1020–1024, September 1946. 15 refs.

Diagnosis

16. **The Xenopus Pregnancy Test.**
By R. F. MILTON. *Brit. med. J.*, 2, 328, September 7, 1946. 13 refs.

The xenopus pregnancy test can now be accepted as a reliable method for routine work. The procedure is simple, and consists in injecting urine into the dorsal sac of the female toad *Xenopus laevis*, and watching for the appearance of the eggs. Its rapidity (6–18 hours) and its accuracy have been commented upon favourably. In addition, the toads may be used again in 3 months' time. On the other hand, the test has been criticized on the grounds that when the gonadotrophic excretion is low, as is often the case in early pregnancy, the normal test is not sensitive enough to indicate

cyesis. As a larger quantity of urine kills the toad, the author evolved and here describes a method of concentrating the urine, thus overcoming this difficulty. The whole of the morning specimen of urine is filtered through a long glass tube containing specially prepared and cleansed permutit on to which the gonadotrophic hormone is adsorbed. Elution of the hormone is made with two washings of 5 per cent ammonia, and the combined elutions are inoculated in the usual manner. The technique, which has been used by the author for over a year, gives a positive result if the excretion of the hormone is greater than 500 I.U. a day, " a condition which rarely occurs in the absence of pregnancy." This method may also be used in a quantitative manner by graduation of the dose.

E. M. Darmady.

17. **Frog Test (Xenopus Laevis) for Pregnancy.**
By C. B. SANDERS. *Tex. St. J. Med.*, 42, 375–376, October 1946.

Examination

18. **The Use of X-rays in Obstetrics plus a Presentation of some Medicolegal Aspects.**
By L. J. GELBER, *Med. Rec., N.Y.*, 159, 663–667, November 1946. 14 refs..

Nutrition

19. **Vitamins in Obstetrics and Gynaecology.**
E. Y. YANKELEVICH. *Pediat. Akush. Ginek.*, No. 4, 24–32, 1946.

This article is a summary of the properties and dosage of and indications for the administration of vitamins A, B_1, C, D, E, and K in obstetrics and gynaecology. It is stressed that the pregnant woman requires two or three times the normal number of units. The author considers that particularly important are: (1) vitamins A, B_1, C, D in both normal and abnormal pregnancy and in the puerperium (an interesting observation is that in spontaneous abortions only 20 per cent of foetal livers were found to contain any vitamin A, while in abortions induced artificially 100 per cent of foetal livers contained a store of vitamin A); (2) vitamins B_1 and K immediately before and during labour; (3) vitamins C and K in haemorrhagic disease of the new born; and (4) vitamins A, C, and K in gynaecology, especially in the treatment of uterine haemorrhages and cervical erosions.

N. Tereshchenko

20. **Weight Control, Diet and Fluid Balance in Pregnancy.**
By C. H. LOUGHRAN. *Amer. J. Obstet. Gynec.,* 52, 42–53, July 1946. 4 figs, 7 refs.

The majority of women who gain weight excessively in pregnancy develop toxaemia or dystocia. Those who gain little weight have a shorter labour and fewer obstetrical complications. Deprivation has little effect on the weight of the baby. Pregnant women need more protein than normal. Exercise is important for body function. The effect on the mental well-being of the patient is important.

A regime of weight control in pregnancy has been employed in 325 consecutive private cases. At first, a total gain in weight of 20 lb. (9.0 kg.) was allowed, but this was later reduced to 15 lb. (7.7 kg.). In obese patients the ideal was no gain at all. A diet high in protein, green vegetables, fruit, and milk, but low in carbohydrate was given with vitamin supplements. Salt was restricted in the later months. Patients gaining beyond their allowance were put on a 1,200 calorie diet. Fluids were restricted in cases with a sudden gain in weight. If oedema and hypoproteinaemia occurred, the patient was admitted to hospital and put on a very high protein diet, supplemented with infusion of plasma.

Results in the 325 cases showed only 2 patients who developed oedema, 1 with heart disease and 1 with nephritis. There was 1 case of post-partum eclampsia, but the general incidence of toxaemia was greatly reduced. There was a marked reduction in obstetrical complications. There were no maternal deaths but 5 stillbirths (a rate of 1.53 per cent), none being attributable to delivery. There were 2 neonatal deaths. A definite relationship is shown between the amount of weight gained and the length of labour and the occurrence of dystocia. A similar relationship between weight gained and the incidence of toxaemia is demonstrated. The author considers that the earliest evidence of toxaemia is an excessive gain in weight, and that a regime of weight control in pregnancy will reduce the incidence of this and other complications of pregnancy and labour.

Josephine Barnes

21. **The Effect of Antenatal Conditions on the New-born Child. I, Maternal Diet. II. Nutritional State of the Mother. III. The Health of the Mother.**
By L. G. PARSONS. *Canad. med Ass. J.,* 55, 327–336, October 1946.

22. **Some Observations on the Role of Protein in Pregnancy.**
By E. M. BLAIR. *West. J. Surg.,* 54, 288–293, July 1946. 12 refs.

See also Nos. 6, 7.

ABNORMAL

Toxaemias

23. **Genetical Antigenic Incompatibility as a Possible Cause of the Toxaemias Occurring Late in Pregnancy.**
By H. KALMUS. *Ann. Eugen., Camb.,* 13, 146–149, August 1946. 6 refs.

If eclampsia is like erythroblastosis foetalis in being dependent on an antigenic incompatibility between mother and foetus, certain peculiarities should occur in the pedigrees of affected women. For instance, a woman who, as a foetus, caused toxaemia in her mother, will only rarely have it herself, while a woman who herself has toxaemia is unlikely to have caused it in her mother. A man who, as a foetus, has caused toxaemia in his mother is relatively likely to cause it in his wife; and conversely, the husband of a toxaemic woman is relatively likely to have caused toxaemia in his mother. Toxaemia should be likely to recur in subsequent pregnancies. Toxaemia would always be more frequent in the sisters of a toxaemic woman, and in her husband's brothers' wives than the general population [little attention has been paid to the latter degree of relation in previous genetical studies]. Other peculiarities of the pedigrees would depend on the relative frequency of the antigen in question, if such in fact should exist.

[The direct evidence for or against the existence of an antigenic difference to account for eclampsia is so far very scanty. The paper draws attention to the points which should be kept in mind in collecting critical data on the problem.]

H. Grüneberg

24. **An Investigation of the Human Placenta for Pressor Substance.**
By T. E. T. BRADSHAW. *Irish J. med. Sci.,* 235–241, July 1946. 14 refs.

The author first discusses the current hypotheses concerning the production of pressor substance, hypertensin (angiotonin), by the interaction of renin with hypertensinogen (globulin). He con-

cludes that renin is present in normal mammalian kidneys and that rendering a kidney ischaemic releases renin into the blood stream producing hypertension: The experimental work deals with an investigation into the possibility that renin might be present in the placentae of cases of eclamptic toxaemia. Its liberation might be responsible for the rise in blood pressure.

Pig-kidney extracts were prepared to ensure that the method of extraction of renin was efficient. Cortices of kidneys were ground to a paste and shaken with alcohol, and the mixture was allowed to stand 24 hours in a refrigerator. Alcohol was filtered off and the residue washed with ether and allowed to dry at room temperature. The ground material after drying was stored in a refrigerator. Placental extraction was made in the same way, 50 g. being used for each extraction. The method of testing for renin was to inject a Ringer's solution extract intravenously into a rabbit and to observe the effect on blood pressure, a rise indicating the presence of renin.

The blood pressure of a non-anaesthetized rabbit (the animal being kept warm) was measured by using a capsule of the design by Grant and Rothschild placed over the central artery of the ear. The systolic blood pressure was measured by raising the pressure in the capsule till the artery just stopped pulsating. The position of the capsule was important as a wide variety of readings was obtained depending on whether the capsule was on the distal or proximal portion of the artery. Material for injection was prepared by shaking a weighed quantity of dried material with Ringer's solution and allowing it to stand overnight in the refrigerator. The material was centrifuged and the supernatant fluid filtered. (The maximum amount injected was 1 ml.) Before testing a sample, blood pressure readings were taken till constant, usually after about 10 minutes. Six different kidney extracts prepared from 0.6 to 1 g. dried kidney powder extracted with 10 ml. Ringer's solution all showed the presence of renin. Placental extracts from normal pregnancies occasionally caused a minor ill-sustained rise in blood pressure. Renin was presumed not to be present. Placental extracts from cases of pre-eclamptic toxaemia also did not cause a rise in blood pressure and there was, therefore, no evidence of the presence of renin in these extracts.

J. Dawson

25. Spontaneous Rupture of the Liver in Eclampsia with Fatal Hemoperitoneum.
By S. SANES and C. A. KAMINSKI. *Amer. J. Obstet. Gynec.*, 52, 325–329, August 1946. 3 figs., 4 refs.

The authors describe a case of eclampsia which terminated fatally from rupture of the liver. The disease was typical in all respects, occurring in a multiparous negress at about the thirtieth week of gestation. Treatment was on the usual lines with intravenous glucose, magnesium sulphate, morphine, and a salt-free diet. Labour was induced by insertion of a bougie, rupture of the membranes, and packing the vagina. The only abnormal feature was the rapidity of delivery, 12 hours later, when the foetus, bougie, and plugging were expelled by one strong sustained contraction. After delivery the patient appeared drowsy, her general condition deteriorated, and collapse and death occurred 16 hours later with signs of internal haemorrhage. Necropsy revealed the usual changes of eclampsia with, in addition, a massive intraperitoneal haemorrhage originating from a rupture of the anterior superior capsule of the liver. The liver in this region was covered by a large subcapsular haemorrhage. The final precipitating cause for the haemorrhage is discussed, and it is suggested that the rigidity of the costal margin may have a bearing on the site of the lesion. Five similar cases from the literature are abstracted, and in each of which rupture of the liver occurred from diffuse subcapsular haemorrhage.

R. B. K. Rickford

26. Necrosis of the Adrenal Cortex and Anterior Lobe of the Pituitary in Pregnancy. (Uber Nierenrinden- und Hypophysenvorderlappennekrose bei Gravidität. Ein Beitrag zur Morphologie der Eklampsie.)
By W. HÜGIN. *Gynaecologia*, 121, 269–287, May—June 1946. 4 figs., 74 refs.

Renal cortical necrosis is a well-recognized complication of pregnancy, and the author reviews the literature of 50 of the recorded cases and also that relating to necrosis of the pituitary gland. He describes 2 cases in detail of the association of both lesions, a condition hitherto unrecorded. In each case there was antecedent toxaemia of pregnancy; eclampsia developed in one patient, while the other had premature detachment of a normally-sited

placenta. There was subsequent anuria, and the patients died in spite of decapsulation of the kidneys. Pathologically, necrosis of the renal cortices and anterior lobes of the pituitary was found, the changes being less pronounced in the eclamptic patient. Besides necrotic changes in the epithelium there was extensive thrombosis and infarction.

Kenneth Bowes

27. Treatment of Eclampsia by Intravenous Magnesium Sulphate Alone. (Traitement exclusif de l'éclampsie par le sulfate de magnésie en voie intraveineuse.)

By M. F. ARMAND. *Obstet. Ginec. latin-amer.,* 4, 410–424, June 30, 1946. 8 refs.

Stroganoff's method of treating eclampsia can be summarized as follows. (1) Narcotics and sedatives —that is, morphine and chloral hydrate—to quieten the nervous excitability and diminish the cerebral oedema. (2) Bleeding and drastic purgatives to eliminate the general oedema. (3) Glucose-serum to combat the intoxication. His results are good, maternal mortality being reduced to 2.6 per cent, and infant mortality to 16 per cent. Lazard's method consists in : (1) Intravenous injection of magnesium sulphate (10 per cent solution) in doses of 20 ml. when the patient's condition requires it, up to a maximum of 90 ml. (2) Extraction of the foetus by forceps if the woman is in the second stage of labour. (3) Oxygen inhalations after each fit. (4) Caesarean section if necessary. (5) Intravenous glucose-serum in 10 per cent strength if there is little oedema, in 50 per cent strength if there is much oedema. His results are also very good, maternal mortality being 0.6 per cent, and infant mortality 46.6 per cent. Browkin's method is more complicated : (1) Intramuscular injection of a 30 per cent solution of magnesium sulphate, 20 ml. at a time, up to 5 injections in the 24 hours. (2) Nothing to drink by the mouth except a little very sweet water. (3) Intravenous injection of 100 ml. of 10 per cent glucose-serum if coma occurs. (4) Administration of saline purgatives. (5) Lumbar puncture. (6) Ether anaethesia for the injections if the patient is very restless. (7) Application of forceps as soon as possible, and extraction of the foetus. (8) Bleeding if the fits are severe. His results are excellent; the maternal mortality is 2.1 per cent and the infant mortality 6.1 per cent.

As the pathology of eclampsia is that of severe water intoxication aggravated by spasm of the arterioles; the author considers that rational treatment consists in employing a powerful antispasmodic and diuretic drug. Magnesium sulphate is the ideal substance for the purpose; it effectively reduces the blood pressure, it produces diuresis rapidly, and reduces oedema of the tissues through its hygroscopic action; it has in addition a narcotic and anaesthetic effect with the advantage of not paralysing the uterine musculature. Finally it does not reduce the alkaline reserve of the blood. The author uses a 50 per cent solution, and injects intravenously 10 ml. (5 g. of salt) of the solution as soon as eclampsia or a pre-eclamptic state is diagnosed, followed by 5 ml. of the solution (2.5 g. of the salt) every 4 hours until return to normal. He also advises a daily dose of 5 ml. so long as headache is present or the blood pressure remains high or tends to rise. The solution must be injected very slowly after being mixed with an equal amount of the patient's blood. The patient frequently complains of a feeling of general warmth, and exhibits slight excitement; this disappears on momentarily stopping the injection, and resuming it more slowly than previously. Sweating often occurs very rapidly, and urine is passed within half an hour; the blood pressure falls immediately by 30 to 60 mm. Hg. No sedatives or any other drugs are given, and no anaesthetic is necessary to control the convulsions; the action of magnesium sulphate in that respect is instantaneous.

A full account of 21 cases is given. Seventeen patients were actually having convulsions on admission, 5 of them being in coma. Eighteen were primiparae and 3 multiparae. Five patients developed eclampsia during pregnancy, 4 during labour, and 12 in the puerperium. There were no maternal deaths; in the 5 cases treated before labour, 3 infants survived and 2 died; in the 4 treated during labour, 2 infants were stillborn, the other 2 survived. The largest total dose of magnesium sulphate injected intravenously exceeded 50 g. There were severe reactions in 3 cases only (shock and syncope, responding rapidly to injection of camphor in oil), all of which had a high blood chloride.

N. N. Tereshchenko

Abortion, Hydatidiform mole

28. **Sodium β-Glycerophosphate in Obstetrics.**
(Betagliceröfosfato sódico ÿ obstetricia.)
By M. RONCALES CATIVIELA. *Farmacoter actual.*
3, 474–478, July 1946. 14 refs.

The author reports 25 cases of threatened abortion treated with sodium beta-glycerophosphate, which acts by inhibiting uterine tone. The treatment was effective in 19 out of the 25 cases. The dose was 10 ml. of a 50 per cent solution injected intravenously. Repeated doses were given without evidence of toxic effects. The uterus remained sensitive to the action of oxytocin and the liquid extract of ergot.

H. M. Adam

29. **The Aetiology of Spontaneous Abortion.**
(Etiologie de l'avortement spontané (en dehors de la syphilis.)
By R. L. ROCHAT. *Gynéc. Obstét.*, 45, 299–336, 1946. 86 refs.

30. **Hydatidiform Mole, with Special Reference to Recurrence and Associated Eclampsia.**
By L. C. CHESLEY, S. A. COSGROVE, and J. PREECE. *Amer. J. Obstet. Gynec.*, 52, 311–320, August 1946. 79 refs.

In this paper the authors describe a case of recurrent hydatidiform mole with severe toxaemia on each occasion. The literature on this association is exhaustively reviewed. Finally, 57 consecutive cases of hydatidiform degeneration of the chorion occurring at the Margaret Hague Maternity Hospital, Jersey City, U.S.A., among 75,238 deliveries (1 in 1,321) are analysed.

The case described is one in which the first pregnancy resulted in a hydatidiform mole, complicated by severe pre-eclampsia. Three normal pregnancies followed, one, however, requiring a manual removal of the placenta, and another a Caesarean section for placenta praevia. The fifth pregnancy again led to a hydatidiform mole with eclampsia, followed later by chorionepithelioma. The first pregnancy terminated spontaneously after 6 weeks' hospitalization for severe albuminuria and hypertension. The uterus was explored digitally after delivery. The Friedman test was negative 2 weeks after delivery, but was positive 3 months later. Curettage was carried out but revealed nothing more than "chronic endometritis". The fifth pregnancy, complicated by 5 eclamptic fits, was terminated by a bag induction followed by digital clearance of the

uterus. The Friedman test was negative 3 weeks later, but weakly positive at 5 weeks. Curettage confirmed the presence of "atypical chorionepithelioma" and a panhysterectomy was carried out. Both ovaries were enlarged and cystic, and one had undergone torsion and was degenerated. [No microscopy of the ovaries is reported.] Ten months later the patient was very well, but was unfortunately accidentally killed with her whole family on leaving the hospital.

The authors in their review of the literature found 40 cases of recurrent hydatidiform mole, and 35 cases of this type of pregnancy complicated by eclampsia. Of the 57 cases occurring at the Margaret Hague Maternity Hospital, 21 per cent were diagnosed before expulsion of vesicles. In 4 cases cystic ovaries were present. An analysis of the symptoms revealed that 96.6 per cent were complicated by bleeding. The uterus was either larger, of normal size, or smaller than expected, in about an equal number of cases. The Friedman test was positive in all cases tested (11), and positive in dilutions up to a maximum of 1 in 9,000 in the cases where this test was applied. Pre-eclampsia occurred in 9 out of the 25 cases over 16 weeks pregnant, but was absent in the 32 patients with a shorter gestation. Five moles were removed abdominally, 4 manually, 13 by curettage, 1 by sponge stick, and the rest were expelled spontaneously. The Friedman test became negative at varying dates postpartum, the latest not for 7½ months. In one case it was positive in dilution of 1 in 50 as late as 4 months after, without the presence of malignancy. Three cases only were followed by chorionic carcinoma [a percentage considerably lower than is usually expected]. In one of these (reported in this paper) the pregnancy test was only weakly positive.

[This is an excellent and interesting paper on the subject of hydatidiform mole and chorionepithelioma. The diseases are rare and dramatic. It should always be remembered when dealing with toxaemia of pregnancy occurring before 16 weeks that there is a great probability of the presence of a hydatidiform mole.]

R. B. K. Rickford

Association with Systemic disease

31. **Thyrotoxicosis and Pregnancy.**
By R. C. STEPTO *West. J. Surg.*, 54, 317–319, August 1946. 18 refs.

32. Diabetes mellitus and Pregnancy: a Review.
By N. J. EASTMAN. *Obstet. Gynec. Surv.*, 1, 3-31, February 1946. 98 refs.

Association with infections.

33. Syphilis in Pregnancy: Preliminary Report on a Tyneside Investigation.
By W. V. MACFARLANE. *Publ. Hlth., Lond.*, 59, 181-185, September 1946. 6 refs.

In 1943 a scheme was introduced in Tyneside whereby all pregnant women attending antenatal centres were encouraged to undergo a Wassermann test. Those in whom a positive result was reported were advised to attend a venereal disease department for further examination. A diagnosis of syphilis was not made until there was a persistent, strongly positive reaction. The syphilitic pregnant women thus discovered, most of whom attended in the later months of their pregnancy, were then placed on a routine treatment of 10 injections of neoarsphenamine and 10 injections of bismuth metal suspension.

In the years 1944 and 1945 the number of live births recorded in Tyneside was 52,000, and 80 per cent of the mothers had attended at an antenatal centre. On account of war-time difficulties the Wassermann test was actually performed on only 24,638 of the women; it is of interest to note that about 1 per cent of the women refused the test. A strongly positive reaction was obtained in 201 women, and in a further 68 it was doubtful; approximately half of the latter number were subsequently found to be non-syphilitic. The number of women who were referred to a venereal diseases clinic was 175, but the report deals mainly with the further history of the 115 who actually attended. Twelve women were still pregnant at the time of reporting, and are excluded from the analysis.

In an attempt to discover why some women failed to co-operate with the clinic the author points out that 84 of the 103 women were in the asymptomatic latent stage of syphilis, in which the absence of symptoms might well make it difficult for them to realize the need for treatment. The highest defaulter rate was experienced in the 22 to 25 age-group, though the incidence of default did not vary in proportion to the different ages. Both these factors may have had some influence on the rate of default; they do not fully explain it. Excluding 16 women who attended too late in pregnancy to re-

ceive adequate treatment, there were 87 who had the opportunity to avail themselves of it, but only 37 did so, in spite of very active efforts at follow-up (tabulated in detail) by the local authorities' health visitors and by the staff of the venereal diseases social departments. Another reason for irregular attendance suggested by the figures given, although not stressed by the author, is the comparatively late stage of pregnancy of many women on first attendance at the venereal diseases clinic. The report contains tables of the outcome of the pregnancy in the 103 women, and the results of adequate and inadequate treatment are contrasted. Some dissatisfaction is expressed at the results of the scheme, and reasons for default and measures to improve co-operation by the patient are discussed. When repeated voluntary efforts have failed compulsion would appear to be the only solution to the problem of default.

[The word " default " is here used as relating to the interruption of regular attendances at the venereal diseases clinic. Sixty out of the 175 women having a positive Wassermann reaction who were referred to a venereal diseases clinic did not attend there at any time. The further steps taken and the difficulties encountered with these " primary losses " are not made clear in the report.]

V. E. Lloyd

34. The Prevention of Syphilis in the Newborn.
By C. N. FRAZIER. *Tex. St. J. Med.*, 42, 372-374, October 1946. 14 refs.

See also Nos. 21, 48-52.

LABOUR

35. The Risks of the Induction of Labour by Aburel's Method. (Los riesgos de la induccion del parto con el metodo de Aburel.)
By M. L. PÉREZ and E. M. BALDI. *Rev. méd.-quirúrg. Pat. fem.*, 25, 179-192, June 1946. 3 figs., 45 refs.

Among the numerous methods of induction of labour that of Aburel (intra-amniotic injection of hypertonic saline) has recently found favour and has been described as relatively safe for mother and foetus. Several disasters have been reported, however, and a list of these is given. Foetal death seems to be the commonest, and the author concludes that the method is risky to the foetus.

Twenty-five cases of induction of labour by Aburel's method are described. In these there were 11 foetal deaths. Three cases are described in detail. In the first, induction was undertaken after the death of the foetus. The mother died, and at necropsy an intense necrosis of the uterine muscle was found, with evidence of acute inflammation. There was also a peritonitis. It is suggested that the solution was inadvertently injected into the uterine muscle. In the second case, one of eclampsia with intrauterine foetal death, the mother also died of peritonitis. In the third case, one of eclampsia, the child was born with a gangrenous condition of the right foot. It is concluded that this is a dangerous method of induction, but that the danger may come from the solution used. Other solutions, such as 25 per cent glucose, should be given clinical trial before the method is abandoned. [Intra-amniotic injections have never found favour in Britain for the induction of labour. It is well that the inherent dangers of the method, some not apparent and thus only discovered after clinical trial, should be made known.]

Josephine Barnes

36. Effect of Antispasmodics on Dilatation in Labour. (Einwirkung von Spasmolytica auf die Eröffnungsperiode bei der Geburt. (Untersuchung eines neuen Mittels " Hexacompal ".))

By H. SAUTER. *Gynaecologia*, 121, 247–268, May–June, 1946. 18 figs., 4 refs.

The effects of pethidine, spasmalgin, and a new preparation, " hexacompal ", on spastic conditions of the uterus in the first stage of labour were studied by the author. Hysterotonography was used particularly to show the actions of the drugs on the amplitude of the contractions, the effect on the tonus during the phases between contractions, and the regularity of the contractions. Hexacompal was deemed to have the best action. It contains papaverine, extract of belladonna, allobarbitone, caffeine, and dimethylaminoantipyrine, i.e., it is allied to spasmalgin, but contains no pantopon. Administered rectally by suppositories [no dosage given], its effect becomes well marked in 10 to 15 minutes, and action is sustained for an hour or longer.

The indications for its use are non-dilatation of the os in the presence of good pains, a rigid cervix, painful contractions, and pain continuing between the contractions. Hexacompal made these spastic conditions disappear rapidly, and the first stage of labour was accelerated. There were no secondary effects noticed on either mother or child. The tonus of the uterus between pains was noticeably greater with hexacompal than with pethidine or spasmalgin. Contra-indications to the use of the drug were premature pressure on the deeply engaged head and induction of labour with poor contractions.

Kenneth Bowes

37. The Effect of Pethidine on Labour. (L'effet de la dolantine sur l'accouchement.)

By F. DE SENARCLENS. *Gynaecologia*, 121, 225–246, May—June 1946. 54 refs.

Pethidine is a synthetic substance combining an anti-spasmodic action of a neurotropic type with an analgesic action like that of morphine. By its vago-depressive action it is particularly useful in helping dilatation of the uterine os. Since Benthin used the product in 1938, and published his observations in 1940 (*Dtsch. med. Wschr.*, 28, 760), various papers on the subject have appeared, and most authorities have been in favour of its use as it has little adverse effect on the baby. Erbslöh (*Zbl. Gynäk.*, 1943, 14, 578), however, does report 4 cases of marked asphyxia in 250 confinements in which pethidine was used.

The author follows Döderlein's technique, injecting 100 mg. intramuscularly and repeating this dose if necessary later, but not within 4 hours. It should not be used late in the second stage of labour. It was given in 167 cases, 127 being primigravidae, and 40 multigravidae. Sixty-one patients were below 25 years old, 85 from 26 to 35, and 21 over 35. A detailed analysis is given of their skeletal types, external pelvimetry, etc. Cases included pelvic contraction, and diseases coincident with pregnancy.

The author concludes that in normal labour pain was considerably relieved and labour accelerated. He tried the preparation particularly in cases of rigid os, abnormal contractions of the lower segment, and when the contractions were too frequent or prolonged. He was impressed by its effect in spastic conditions. There were no marked untoward effects. One baby had white asphyxia and one blue. An oxytocic was needed as well for 13 per cent of the patients. Additional anaesthesia proved no handicap. No observation is made in regard to third-stage bleeding.

Kenneth Bowes

38 The Clinical Diagnosis of Varying Degrees of Uterine Contraction Rings.

By H. W. JOHNSON. *Amer. J. Obstet. Gynec.*, 52, 74–82, July 1946. 7 figs., 5 refs.

An apparent difference in the incidence of uterine contraction ring as a cause of dystocia is found between the author's practice and the practice of two hospitals in Houston, Texas, the difference being due to the author's greater interest in, and awareness of, the condition. It is well known that a physiological ring develops in normal labour at the junction of the upper and lower uterine segments. The terminology of the pathological varieties remains confused and bewildering. The author accepts the classification given in the *Standard Nomenclature of Diseases and Operations*, and is convinced that rings occur in both obstructed and unobstructed labours, and when present are obstacles to the progress of labour.

In the first group obstruction to the passage of the foetus causes development of contraction ring, and the degree of ring formation is dependent on the degree of obstruction. In the second group the ring causes obstruction to the passage of the foetus. It is with the second group that the author is mainly concerned, and he divides them into mild and severe. The mild type may develop early in the first stage of labour or not until almost the end of the second stage. Premature rupture of the membranes is believed to predispose to this condition. Diagnosis is made on account of the colicky nature of the pains, and in cases where the ring forms early in labour on the fact that the cervix does not dilate. The author emphasizes that "the cervix will always dilate when labour pains are adequate but only very slowly in unobstructed labours where a contraction ring is forming or has formed." Later the diagnosis may be confirmed by passing a finger through the cervix, between the uterine wall and the head, and noting that when the upper part of the uterus contracts strongly the impact on the examining finger is weak.

Treatment is expectant until the cervix is 4 cm. dilated. Then the patient is anaesthetized, episiotomy is performed, the cervix pushed gently over the head, and the lower segment explored. If no loop of cord is encountered mid-forceps is applied and delivery accomplished, with deepening of anaesthesia if necessary. If the cord is present in the lower segment, version and extraction are performed. Adrenaline is useless for this type of ring, but deep ether or chloroform anaesthesia will relax it.

[Amyl nitrite, which has been used with success in treatment of contraction ring, is not mentioned in this article. It is doubtful whether such radical methods of treatment as those outlined for the treatment of mild cases of contraction ring dystocia would find favour in most clinics.]

Josephine Barnes

39. Use of Methergine in the Third Stage of Labour. (Effets et rôle de la méthergine au cours de la période placentaire de l'accouchement.)

By J. P. D'ERNST. *Schweiz. med. Wschr.*, 76, 775–777, August 24, 1946. 7 refs.

It was shown by Jacobs and Craig in 1934 that the products derived from ergot of rye all contain a particular acid, which they named lysergic acid. Methergine is a new, semi-synthetic substance, methylergobasine (methylergometrine) M.E. 277 (2-butanol-amide of *d*-lysergic acid).

An outline is given of the methods in current use for the management of cases of post-partum haemorrhage at the Obstetrical Clinic at Geneva. Ergometrine (known as basergine in Switzerland) was extensively used and was found to act rapidly, but its action was of short duration. If given before the birth of the placenta, it rarely led to satisfactory delivery, and symptoms of intolerance, such as headache, vertigo, and vomiting, were often seen. Methergine was given a clinical trial in 100 cases, as a possible alternative to ergometrine. It was given in a dose of 0.2 mg. either during the passage of the head over the perineum, or at the moment of appearance of the anterior shoulder, or immediately after the birth of the child. The injection was given intravenously whenever possible, and before the birth of the child. Observations were on the amount of blood loss, on the interval before contraction of the uterus, and the interval before delivery of the placenta. It was found that the uterus contracted briskly 35 to 50 seconds after injection in most cases, that the average duration of the third stage of labour was 8 minutes 6 seconds, and that the average loss of blood was 176 ml. It was found that the usual signs of placental separation were absent, but that in spite of this, delivery was easily accomplished in every case. Retention of placental cotyledons was not seen, though reten-

tion of membranes occurred in some cases. No symptoms of intolerance were found, and the puerperium was comparable to that experienced by a control group of women delivered of the placenta spontaneously. Methergine is contra-indicated in cases where a moderate loss of blood may be considered advantageous, including cases of severe toxaemia with high blood pressure, eclampsia, and renal disease with hypertension. In twin pregnancy, the injection should not be given until after the birth of the second infant. Intramuscular injections gave much less satisfactory results.

It appears that the administration of methergine for prevention of post-partum haemorrhage is a useful procedure and that it is one worthy of extended trial. Many substances have been introduced in an attempt to shorten the third stage of labour and to diminish post-partum haemorrhage. In Britain the general feeling is against using oxytocic drugs before the birth of the placenta, though some use oxytocin, and others even ergot preparations. The chief complication feared is contraction ring. This has not occurred in the present series with methergine but the numbers are small, and clearly more extended trials are needed, under expert supervision, before the method can safely be recommended for routine use."

Josephine Barnes

40. A Placenta Accreta.
By E. H. Stander. Med. Rec. N.Y., 159, 677–678, November 1946.

ANAESTHETICS, ANALGESIA

41. Intravenous Pentothal Anaesthesia in Obstetrics, with Pitocin Injections. (Accouchements sous anesthésie au pentothal intraveineux avec pitocin.)
By H. A. Bourdeau. Un. méd. Can., 75, 903–906. August 1946. 5 refs.

A case is described in which intravenous pentothal was given late in labour and followed with a dose of pitocin. The result was a rapid delivery with immediate recovery of consciousness. It was decided to try the method in a series of cases. A small dose of pentothal was found to enhance uterine contractions, larger doses, however, caused them to cease. There was amnesia after pentothal. In a case it was found that profound anaesthesia with cessation of uterine contractions appeared.

Two injections of 1 ml. each of pitocin were given without effect. Later 5 ml. of a 1 in 20 solution of pitocin was given intravenously, with the result that 3 contractions occurred and a low-forceps delivery was possible. After this the pentothal and pitocin were mixed in one syringe, 1 ml. of pitocin to each 20 ml. of a 2.5 per cent solution of pentothal.

The method was tried in 259 cases, including 69 primiparae. Results were good—no maternal mortality and only 3 foetal deaths. The injection was begun when the os was fully dilated, or dilatable. The first injection was of 5 to 8 ml., and this was repeated up to 3 times if necessary. Episiotomy was performed in primiparae, and forceps applied after the third injection if delivery had not taken place. Forceps delivery was required in 19 out of the 69 primiparae. The third stage of labour was usually rapid. Contra-indications included inability of the cervix to dilate, non-engagement of the head, any obstruction to normal delivery, and the previous use of another barbiturate. Advantages claimed are that anaesthesia and analgesia were rapid, delivery expeditious, recovery rapid, and the anaesthetic non-inflammable. Disadvantages include the necessity to await full dilatation and the risk of rupture of the uterus.

This appears to be a highly dangerous method of conducting labour, in spite of the good results claimed in a relatively small series of cases. The depressing effect of pentothal on the foetal nervous system is well known. The forceps rate in primiparae is nearly 30 per cent, and the author admits, though with some qualification, the risk of uterine rupture. These are only 3 of the many possible dangers inherent in the method. There are better and safer ways of conducting normal labour with satisfactory analgesia and anaesthesia when required."

Josephine Barnes

42. Intravenous Procaine for Obstetrical Anaesthesia.
By H. Johnson and C. R. A. Green. Curr. Res. Anesth., 25, 133–145, July-August 1946. 3 refs.

There are two stages in intravenous procaine for obstetrical anaesthesia: (1) Small dose; rate of infusion usually about 2 ml. per minute of 1 per cent solution (varied from 0.5 to 1.6 ml.); patient remains conscious and mentally clear; pain is much

reduced or abolished. (2) Large dose; rate of infusion usually 16 to 20 ml. per minute; pain is abolished; patient is semi-conscious and usually co-operative.

Twenty labour cases are described by the authors, the ages of the patients ranging from 15 to 31 years. Eighteen of them had nembutal per os; the 2 who did not were admitted late in labour, and were started immediately upon large-dose procaine infusions. The others were started upon small-dose infusions, their stage of dilatation ranging from 1 to 8 cm. The authors recommend a barbiturate as a preventive for the tendency to convulsions caused by intravenous procaine. All the children were born living, and only 1 required resuscitation, and that was in the case which had the smallest total dose of procaine (0.3 g.). Quick recovery (about 5 minutes after large doses) and lack of after-effects were striking features. Very large total amounts were used. Seven of the cases had over 5 g. and the largest dose was 9.7 g. The usual procedure was for the small-dose method to be used in the earlier stages of labour, and then, when delivery drew near, for the flow to be quickened until semi-consciousness and mental confusion were produced. Immediately after the end of the second stage the patient was allowed to recover, but the anaesthesia was deepened again if repair of the perineum or repair of episiotomy was needed. Six of the patients had some symptoms of toxaemia, 4 of these had twitchings of the face during the rapid infusion. In 2 the method was abandoned for fear of convulsions, ether being given for the delivery. One of them had post-partum eclampsia.

In all cases a 1 per cent solution was used. Procaine 10 g. was dissolved in a little water, sterilized, and then made up to 1 litre with 5 per cent glucose solution. This is used instead of saline to avoid risks of oedema. Every patient is tested for procaine sensitiveness by injecting a drop of 2 per cent solution intradermally and waiting at least 15 minutes; if the result is negative or doubtful a drop can be instilled in one eye for further verification if desired.

The authors state that the 20 cases described, added to the 12 previously reported, make up a series of 32 without a death or serious accident; that though this experience is encouraging as regards safety to mother and child, it is obviously a small basis for recommendation of a new anaesthetic method, and prudence and reservation are still necessary; and that the simplicity of the method makes it available to every physician.

[The authors describe their test for procaine sensitivity, but give no indication of what happens if the test is positive. They also do not mention a difficulty which one would think likely to occur—i.e., the difficulty of keeping a needle in a vein for many hours during the various stages of labour.]

W. Stanley Sykes

43. **Analgesia in Obstetrics: A Comprehensive Review.** (L'analgésie obstétricale.)
By J. SNOECK and M. ROCMANS. *Gynéc. Obstét.*, 45, 257–287, 1946. 5 figs., 38 refs.

PUERPERIUM

44. **The White Cell Count and the Sedimentation Rate in the Uncomplicated and Afebrile Puerperium.** (Untersuchungen über das Verhalten des weissen Blutbildes und der Blutsenkungsgeschwindigkeit im fieberfreien ungestörten Wochenbett.)
By F. PERABO. *Gynaecologia*, 122, 16–52, July-August, 1946. 7 figs., 42 refs.

Variations in the leucocyte count, sedimentation rate, and haemoglobin percentage of the blood were observed in 200 cases of the uncomplicated and afebrile puerperium. Examinations were made before delivery and on the fifth, ninth, twenty-first, and forty-second days postpartum. Statistically the results were examined by the arithmetic mean, the mean quadratic deviation, and the variation coefficient. Before delivery the white cell count averaged 12,100 per c.mm. This fell to 7,900 on the fifth day and to 6,900 on the ninth. A rise of 1,000 per c.mm. during the puerperium proved an indication of some casual complication and was never a sign of the puerperal state itself. In general there was a similar response in the differential cell count though the lymphocytes fell to about half their proportion present before birth. A drift to the left in the white cell count before labour was rapidly compensated for in the puerperium. The sedimentation rate rose to 50 mm. before labour and was followed by a slow restitution in the puerperium with a value of up to 15 mm. 6 weeks postpartum. The haemoglobin averaged 80 per cent before delivery and 75 per cent on the fifth day of the puerperium. The influence of the haemoglobin value on the sedimentation rate was not obvious.

R. K. Bowes

45. **Puerperal Infection.**

By J. H. E. WOLTZ. *Amer. J. med. Sci.*, 211, 743–751, June 1946. 81 refs.

46. **Pathogenicity of Group C (Lancefield) Haemolytic Streptococcus.**

By R. I. HUTCHINSON. *Brit. med. J.*, 2, 575–576, October 19, 1946. 6 refs.

One hundred and five Group C strains of haemolytic streptococci were recognized among 970 groupable strains isolated in a Public Health Laboratory in 2 years. Thirty-two were derived from healthy throats, 4 from healthy vaginae, and the remainder as follows: acutely ill cases (septicaemia, cellulitis, septic throat) 9, mild tonsillitis 33, soft-tissue suppuration 12, puerperal genital tract 12, chronic bronchitis 3. In the majority of cases the disease was mild. All strains gave a clear-cut serological reaction with Group C serum and all yielded a soluble haemolysin. Sixteen strains fermented trehalose but not sorbitol, thus resembling Evans's *Str. equisimilis;* of these 16, 4 failed to ferment human fibrin and so were possibly of animal origin. The 30 strains failing to ferment sorbitol or trehalose all lysed human fibrin and differed from *Str. equi.* in various ways.

R. E. O. Williams

47. **Penicillin in Treatment of Acute Puerperal Mastitis.**

By M. D. TAYLOR and S. WAY. *Brit. med. J.*, 2, 731–732, November 16, 1946. 2 refs.

THE INFANT

48. **Rubella and Congenital Abnormalities.**
EDITORIAL REVIEW. *Brit. med. J.*, 2, 778–779, November 23, 1946. 9 refs.

49. **Congenital Cardiac Defects Associated with Maternal Rubella.**

By L. P. WINTERBOTHAM. *Med. J. Aust.*, 2, 10–19, July 6, 1946. 1 fig.

Some statistical indirect evidence is adduced in support of the thesis enunciated by the Australian ophthalmologist N. M. Gregg (*Trans. Ophthal. Soc. Aust.*, 1941, 3, 35) and others that certain cases of congenital cataract, deafness, and cardiac and other defects occur apparently as a result of German measles attacking the mother during the first 4 months of her pregnancy. As rubella is not a notifiable disease reliable information concerning its epidemic prevalence is difficult to obtain. It is known, however, that in Queensland the 2 principal outbreaks of rubella in recent years occurred in 1937 and 1940. The author correlates with this fact: (1) a considerable increase in the number of cases of congenital deaf-mutism in 1938, as shown by the fact that no fewer than 48 new pupils enrolled in the Blind and Deaf School, Brisbane, in 1945, compared with an annual average admission of 7; (2) an increase in the number of deaf children born in 1940 now registering in the school; and (3) the fact that deaths from congenital heart disease in the year 1941 reached the highest figure so far recorded for Queensland. Similarly, in New South Wales, a thirty-fold increase in the number of children absent from school on account of rubella in 1940, as compared with 1939 is correlated with a large increase in admissions to the school for deaf children born in 1941, and with a greatly increased mortality rate from congenital heart disease in the same year. Similar correlations between epidemic prevalence of rubella and increases of deaf-mutism and of infantile cardiac mortality are presented for the states of Victoria, South Australia, and Western Australia. This evidence, as the author remarks, is not conclusive, but presents at least a remarkable coincidence.

A graph illustrates clearly for the State of Queensland the wave of increase in the number of children born deaf which occurred about every fifth year for the past 42 years. The increase for 1941 was high, and for 1938 was enormous, and there is evidence suggesting a correlation with rubella for these 2 years. For earlier years, in the absence of information on the incidence of rubella, the correlation can be by inference only. In view of the importance of the social and economic questions involved it is rightly suggested that further wide investigations should be undertaken. Information is required particularly about apparently healthy children whose mothers are believed to have suffered from rubella in early pregnancy. Thus, in Western Australia, rubella has been made a notifiable disease, and in Queensland a survey is to be undertaken of all school children born in 1941 to ascertain whether the mother had suffered from rubella during that pregnancy, and, if so, what effect it had had on the child.

H. Stanley Banks

50. **Maternal Disease as a Principle in the Epidemiology of Congenital Anomalies, with a Review of Rubella.**

By W. L. AYCOCK and T. H. INGALLS. *Amer. J. med. Sci.*, 212, 366–379, September 1946. 5 figs., 44 refs.

51. **Congenital Cataract and Other Anomalies following Rubella in the Mother during Pregnancy.**

By J. T. PRENDERGAST. *Arch. Ophthalmol.*, 35, 39–41, January 1946.

52. **Some Observations on Congenital Defects following Maternal Rubella.**

By N. McA. GREGG. *Bull. Postgrad. Comm. Med., Univ. Sydney*, 1, 98–105, October 1945.

53. **The Miasm of Marasmus.**

ANNOTATION. *Brit. med. J.*, 2, 497–498, October 5, 1946. 7 refs.

With an increased incidence of enteritis in the general population diarrhoea in mothers and babies has been observed in lying-in hospitals. A typical epidemic occurred in general and maternity wards of a 1,000-bed hospital in May 1945 and was described by Brown, Crawford, and Stent (*Brit. Med. J.*, 1945, 2, 524). During a 15-week period 20 patients had diarrhoea on admission, and 91 persons, including 27 nurses and 25 babies, developed watery diarrhoea while in hospital. There was vomiting in 46 of the total 111 cases, and pyrexia in 32 of the 89 adults. Twenty-five adults had nausea. The outbreak was traced from 2 emergency cases admitted to a surgical ward, through a ward maid, a nurse, babies, mothers, and medical officers. There were no significant bacteriological findings. The disease, which was considered by local doctors to be a new one, was widespread among the adult population. No deaths had occurred. The epidemic was instructive because: (1) The maternity unit consisted of 66 beds and 66 cots in 3 adjacent wards, one of which escaped entirely. (2) All babies were breast-fed, yet often the mother only or the baby only was affected; when both were affected babies showed signs 4.4 days (on an average) earlier than mothers. (3) The outbreak terminated spontaneously without closure of the maternity unit. (4) The severity was not comparable to that of a previous epidemic of neonatal diarrhoea.

Since then, in some of the 1946 outbreaks of this watery diarrhoea in mothers and babies, an appreciable mortality among the babies has been reported—12 out of 77 affected babies in one outbreak. The characteristic orange-coloured stools of the " epidemic diarrhoea of the newborn " have not been described, nor has there been evidence of parenteral infection. Sulphonamides have been ineffective. Some of the babies seemed at first to respond to treatment, then collapsed and died rather suddenly. The diagnosis of " epidemic diarrhoea of the newborn " is difficult to make in the initial cases of an outbreak, and it is wise to treat every infant with diarrhoea or, in fact, sudden loss of weight, as potentially infectious. The term " diarrhoea of the newborn " has in itself little meaning; it describes a clinical entity with a very varied aetiology. Our concept of the causes is not appreciably removed from the " miasm " stage, and careful records with full descriptions of all the clinical and epidemiological features of an outbreak would be of the greatest value in elucidating the problem.

Mary J. Wilmers

54. **Diarrhoea and Enteritis amongst Infants in the London Area, 1930–38.**

By G. PAYLING WRIGHT and H. PAYLING WRIGHT. *J. Hyg., Camb.*, 44, 480–490, September 1946. 19 refs.

55. **Studies of Maternal and Infantile Blood Factor Relationships.**

By L. M. BRYCE, R. JAKOBOWICZ, and N. McARTHUR. *Med. J. Austr.*, 2, 217–224, August 17, 1946. 2 figs., 18 refs.

It is now fully established and widely known that when an Rh-negative woman becomes pregnant with an Rh-positive foetus she sometimes forms anti-Rh anti-bodies and passes them back through the placenta, with resulting damage to the foetus. Nevertheless, knowledge is still incomplete about the frequency with which this occurs, the factors determining its occurrence in one case rather than another, and the role of antigens other than Rh in the process. The present paper records the result of a survey of 2,230 women whose blood was examined during pregnancy. This number has been split up into different groups because some of the women were not followed to term or the blood of their infants was not tested. The most important group analysed was of 850 women who were tested at intervals during pregnancy and followed to term, and whose infants were also tested. In these 850 cases the incidence of damage to the foetus, here defined as stillbirth, prematurity, icterus gravis, mild jaundice, and anaemia, was twice as high (28.6 per cent) in those cases in which the

mother was Rh-negative and the infant Rh-positive as it was in the remaining cases (14.5 per cent). Icterus gravis neonatorum was diagnosed in 10 of the 850 cases; in 4 of these 10 cases the mother was Rh-positive, but there was incompatibility between mother and foetus with regard to the ABO groups. [The authors' assumption that in these cases immunization of the mother to A or B was responsible cannot be accepted unreservedly; there may, for instance, have been Rh sub-group differences which would not have been detected by the method employed, and the test for blocking antibodies (Wiener's) may have failed to detect sensitization to Rh in some of these cases.] In the series as a whole, ABO incompatibility did not cause a significant incidence of damage to the foetus, though the authors believe that it may occasionally cause icterus gravis and, more frequently, a mild form of haemolytic disease, manifested as " late anaemia." Seven of 9 cases of anaemia of the newborn in this series were associated with ABO incompatibility between mother and foetus.

Titration of anti-A and anti-B agglutinins in the mother's plasma showed no changes early in pregnancy, but in over half the cases in which there was incompatibility between the foetal cells and the mother's plasma there was an immune response after delivery. This stimulation only occurred when the infant was a secretor, and then not always. Because of " the widespread popular belief that there is a higher incidence of miscarriages, stillbirths, neonatal deaths, and other obstetric accidents among Rh-negative than among Rh-positive women," two series of women were questioned as to their past history—namely, a group of 200 blood donors (100 Rh-negative and 100 Rh-positive) and a series of 1,379 women, unselected with regard to Rh type, attending an ante-natal clinic. Statistical analysis revealed " no close correlation between such accidents, taken collectively, and the Rh-negative state," although " there was among the Rh-negative women a significantly higher incidence of prematurity, stillbirths, and icterus gravis neonatorum."

[The inclusion of stillbirths among the " obstetric accidents " to which the Rh-negative woman is not especially liable and also among the conditions to which her foetus is especially liable makes this statement confusing. The point seems to be that

only some stillbirths are due to damage of the foetus by agglutinins, and that very few miscarriages are caused in this way. Thus, if miscarriages and stillbirths from all causes are grouped together it will be difficult, except in a very large series, to show that incompatible agglutinins play any part in their aetiology.]

P. L. Mollison

56. Recent Developments in the Knowledge of the Rh-Hr Blood Types: Tests for Rh Sensitization.
By A. S. WIENER. Amer. J. clin. Path., 16, 477–497, August 1946. 2 figs., 76 refs.

57. The Blood Group Rh. I. A Review of the Antigenic Structure and Serological Reactions of the Rh Subtypes. II. Clinical Applications in Transfusion Therapy and in Haemolytic Disease of the Newborn.
By D. F. CAPPELL. Brit. med. J., 2, 601–605, October 26, 1946; 641–647, November 2, 1946. 62 refs.

58. Jaundice in the Newborn Infant.
By G. W. SALMON. Tex. St. J. Med., 42, 366–371, October 1946. 6 figs., 11 refs.

59. Icterus Gravis Neonatorum: End-results of Treatment by Blood Transfusion.
By H. THIRD. Lancet, 2, 635–636, November 2, 1946. 6 refs.

See also Nos. 11, 15, 21.

GYNAECOLOGY

Menstrual disorders.

60. Studies in Nicotinic Acid.
By R. W. HAWKER. Med. J. Aust., 1, 872–876, June 22, 1946.

The history and physiology of nicotinic acid are briefly described. In 1926 it was found that the thermostable portion of the vitamin B complex possessed pellagra-preventive properties; subsequently it was demonstrated that the black tongue of dogs was analogous to pellagra. In 1937 nicotinic acid amide was isolated from liver concentrates; it was found to cure black tongue in dogs, and later pellagra in man. The chief dietary sources are meat, fish, wheat germ, unpolished rice, and yeast. Chemically, nicotinic acid is a pyridine β-carboxylic acid, and the amide forms the prosthetic group of both co-enzymes I and II. Vasodilatation is produced by nicotinic acid and its salts, but not by the amide or diethylamide (nikethamide or " coramine ").

The first section of the paper discusses the influence of nicotinic acid in stimulating the growth and development of primordial follicles in immature virgin guinea-pigs. The experiment lasted 17 days, and at the end of this period the ovaries of the animals treated with oral nicotinic acid showed an increase in weight of 22 per cent over the controls, while the pituitary glands showed a decrease in weight of 20 per cent as compared with the controls. The increase in weight in the treated ovaries was due to the rapid proliferation and ripening of many primordial follicles. The author admits that, as only 4 animals were used, the experiment is inconclusive.

The second section discusses the effects of nicotinic acid in amenorrhoea, hypomenorrhoea, and dysmenorrhoea. Two cases of primary amenorrhoea of ovarian type are described, both responding successfully to nicotinic acid in a dosage of 50 mg. thrice daily. A third case—of a married woman with a small fibromuscular uterus—failed to respond to treatment. Hypomenorrhoea is attributed to insufficient endometrial change, resulting from either insufficient ovarian hormone stimulation or local uterine abnormality, due to defective ovaries, hypopituitarism, or hypothyroidism. Eleven cases are described, all of which were treated with nicotinic acid; success was achieved in 9 with 2 failures. Dysmenorrhoea is divided into two categories: (1) primary, where the cause is not known, and (2) secondary to some pelvic abnormality. Fifteen patients suffering from primary dysmenorrhoea were selected for treatment. Oestrone, 1 mg. thrice daily, had a dubious effect, nicotinic acid, 50 mg. thrice daily, a delayed effect, while the combination of the two drugs was highly satisfactory.

The conclusions to be drawn from this study appear to be that hypofunction of the ovaries will respond to nicotinic acid but it is not possible to say whether the drug acts directly upon the epithelial elements of the ovary, whether it stimulates the immature or under-functioning primordial follicles through the anterior lobe of the pituitary gland, or whether its influence is through the autonomic nervous system. Stress is laid on the rapid weight loss experienced by obese subjects while receiving nicotinic acid and on the fact that when oestrone and nicotinic acid are combined their function is enhanced.

Geoffrey McComas

61. Ovarian Haemorrhage. (Les hémorragies ovariennes non gravidiques.)
By P. MOCQUOT and R. MUSSET. *Gynéc. Obstét.,* 45, 337–358, 1946. 32 refs.

62. Leucorrhea. A Diagnostic Aid.
By D. LAZARUS and E. E. LAZARUS. *Med. Rec., N.Y.,* 159, 672–674, November 1946.

See also Nos. 5, 19.

Sterility.

63. Infertility.
EDITORIAL REVIEW. *Brit. med. J.,* 2, 618–619, October 26, 1946. 6 refs.

64. Childlessness and the Small Family: a Fertility Survey in Luton.
By R. M. TITMUSS and F. GRUNDY. *Lancet,* 2, 687–690, November 9, 1946. 2 refs.

65. An Analysis of 257 Cases of Sterility.
By S. G. WINSON. *Amer. J. Obstet. Gynec.,* 52, 631–635, October 1946. 6 refs.

66. A Mucin-Splitting Enzyme (Hyaluronidase) in Normal and Pathological Semen. (Über ein mucinspaltendes Ferment (Hyaluronidase) in normalen und pathologischen menschlichen Sperma. Ein Beitrag zur Frage der männlichen Fertilitätsstörungen.)
By E. EICHENBERGER. *Gynaecologia,* 121, 288–329, May–June 1946. 6 figs., 114 refs.

Within recent years more attention has been paid to the male factor in sterile marriages. It has been shown that for fertility the number of spermatozoa in the ejaculate must be of the order of 60,000,000 per ml. or more. Spallanzani was the first to point out the importance of this quantitative relation between the sperms and the ovum. Gleichen-Russworm in 1778 was the first to publish systematic sperm analysis, and in 1853 Gosselin showed the relation between gonorrhoea and aspermia. Winter in 1921 summarized the relation of azoospermia to infertility with figures gained from 4 sources, and found 25 to 33 per cent with this abnormality present. Meaker had no cases of fertility with sperm counts of under 60,000,000 per ml., and Walker only 4 out of 294 such patients.

This finding may be related to a mucin-splitting ferment which is important in the fusion of the sperm and ovum. Duran-Reynals in 1928, McClean in 1930, and Hoffman with Duran-Reynals in 1931 demonstrated an aqueous extract from the testes or semen which contained a factor increasing tissue permeability. This was termed a spreading or diffusion factor. In 1939 Chain and Duthie showed the

factor to work by mucolytic action producing an alteration in viscosity due to a ferment action. The ferment has been termed hyaluronidase. To demonstrate its action a basis is made from mucin tissue of synovia, cornea, or umbilical cord. This is prepared by cleansing the material, extracting any blood with acetic acid, which in turn is removed by alcohol and later water of pH 7.0. The mucin is then precipitated with acetic acidulated alcohol. Finally it is dried in a vacuum. The action tends to be specific to mucins obtained from mesothelial tissues—e.g., there is no reaction to salivary or bronchial secretions.

The biological importance was pointed out by Kurzrok and Miller in 1928, who showed that the semen dissolved the cervical mucus plug. The properties of thermolability, pH constancy, etc., favour a ferment action. The action can be nullified by pus in the secretion, hence sterility may result. Kurzrok and Miller also suggested the possibility of a lytic substance which loosens the cells of the corona radiata round the ovum. This was demonstrated experimentally in rats by McClean and Rowlands in 1942 (*Nature*, **150**, 627).

The author set out to demonstrate the presence of hyaluronidase in human semen, and to determine its relation to fertility. He has found an enzyme whose qualities are akin to those of hyaluronidase. In general there is a parallel between the number of sperms in the ejaculate and the enzyme content of the specimen. If there are no sperms there is no hyaluronidase. The method used was viscometric and the substrate was obtained from umbilical cord by McClean's technique.

With this article there is an excellent bibliography of the subject.

Kenneth Bowes

See also No. 10.

Infections of the Reproductive Organs.

67. Infection of the Urinary Tract in the Female due to *Trichomonas vaginalis*.
By B. WILLIAMS. *Brit. J. Urol.*, 18, 63–65, June 1946. 3 refs.

The author believes that *Trichomonas vaginalis* is a common cause of urinary tract infection in young females, and describes 14 cases with urgency, frequency, and scalding on micturition, where *Trichomonas vaginalis* was found in the vagina. In several cases there were rigors, pain in the loins, and temperature up to 103°F. (39.4°C.). In only 1 case were a few active parasites found in a catheter specimen of urine. The urine usually contained many pus cells together with staphylococci or *E. coli* on culture. [The author has not brought forward any evidence, other than in 1 case, to show that the infection was not due to the presence of staphylococci or *E. coli* in the urine.] He considers that *Trichomonas vaginalis* was responsible for the urinary infection in view of its presence in the vagina or vulva. The urinary symptoms usually subsided quickly with rest, fluids, and alkalis, and, in a few cases, after administration of sulphanilamide or sulphathiazole.

The statement is made that it is probable that *Trichomonas vaginalis* is a frequent and common cause of urinary infection in the young female.

A. W. Badenoch

68. A New Method of Treatment for Vaginitis and Cervicitis.
By S. L. SIEGLER. *Amer. J. Obstet. Gynec.*, 52, 1–13, July 1946. 6 figs., 24 refs.

Recent observations have shown the importance of the relationship between vaginal pH and vaginal flora. Jellies, tablets, and powders buffered to pH readings approximating to that normally found in the vagina have therefore been introduced. The ideal vaginal medicament should be easy to apply by the physician, buffered effectively to promote correct acidity and growth of Döderlein's bacilli, antibacterial, of a physical consistency to ensure intimate and prolonged contact with vaginal and cervical mucosa, non-toxic and effective against both bacterial and protozoal infections. The author believes that these conditions are best fulfilled by an acid jelly containing sulphathiazole. The base is polyethylene glycol and a single, disposable paper container is used. Criteria of cure are: complete relief of symptoms, return to normal pH, and negative smears at intervals during three months following the end of treatment.

Of 230 cases of vaginitis from various causes 83 per cent were cured. In 2 cases a rash developed attributed to sulphathiazole. Of 24 cases of trichomonas infection 75 per cent were cured with acid jelly alone, without sulphathiazole. The rest were subsequently cured by changing to sulphathiazole. Gentian violet acid jelly was effective in 28 cases of monilia vaginitis, but failed in 2 cases where sul-

phathiazole acid jelly had also failed. Iodine in the acid jelly base (1 per cent) was effective in 6 cases of trichomonas, but produced a chemical burn in 2 cases and was therefore discontinued.

Sulphathiazole acid jelly was used in 152 cases of cervicitis, either alone or after cauterization. Good results were obtained, there was no offensive odour or foul discharge and the vaginal pH was found to be normal at the end of treatment. There was a marked reduction in healing time. Sulpha-thiazole was shown to be important in these cases and healing was definitely prolonged in cases where acid jelly alone was used. Sulphathiazole-polyethylene acid jelly was also found to control vaginal infections after surgery by the vaginal route.

The chief risk appears to be that of sensitivity to sulphathiazole, but the method has many advantages, including ease of application, which means ready co-operation on the part of the patient. The disposable paper container is especially advantageous in this respect.

Josephine Barnes

69. Cervical Erosion.
By J. D. JOUBERT. *S. Afr. med. J.*, 20, 632–633, October 26, 1946.

70. Does Metritis of Endocrine or Dietary Deficiency Origin Exist? (Existe-t-il des métrites d'origine hormonale ou par carence?)
By J. BRET and J. BALMARY. *Rev. franç. Gynéc.*, 41, 309–318, October 1946.

The authors report on a series of cases of intractable cervicitis and vaginitis which did not respond to any of the orthodox treatments. Not even temporary improvement occurred from injections, local applications, cauterization, or diathermy, in the endocervicitis, cervical erosion, or the abundant purulent vaginal discharge of these patients. There was no evidence of infection by the gonococcus or the *Trichomonas vaginalis*, and the only positive finding was a high cervical and vaginal pH, varying from 6 to 8 (the normal average being 4.6). The ages of the 10 patients reported on varied from 10 to 54 years. Locally all had an inflammation of the cervix, with or without an accompanying vaginitis, the pH being invariably on the alkaline side of normal. Another finding common to all patients was hypomenorrhoea or amenorrhoea, suggestive of ovarian hypofunction. On investigation, all the patients were found to have been under-nourished

for some considerable time, fats and proteins of animal origin especially being lacking in their diets. As ovarian hormones are essential for the proper nutrition of cervical and vaginal mucosae, the authors suggest as a hypothesis that the lack of fats has caused a diminished production of cholesterol in the body, this in turn producing an insufficient amount of sexual hormones, which are apparently synthesized by the body from cholesterol. As additional evidence of this possible explanation, the authors bring forward the observations by Russian medical research workers on women and girls who died of starvation; Graafian follicles were entirely absent from the ovaries of little girls and there were no fully-developed follicles in the ovaries of adult women.

The authors also mention a recent experiment conducted in France, proving that the weight of the pituitary body is diminished in rats kept on a starvation diet, and the finding that there is a diminution in the number of eosinophil cells in the pituitary glands of grossly under-nourished human beings. The authors' treatment of the cases under review consisted of the following: (1) Local—(a) acid vaginal douches, (b) application of an acid cream (pH 4.5) to combat the pruritis usually co-existing with the profuse vaginal discharge. (2) General—(a) diet rich in fats and meat, (b) calcium by injection, (c) administration of vitamin D and irradiation with ultra-violet light, (d) administration of ascorbic acid and fresh fruit, and (e) phosphoric acid administration. In addition, the patients in whom an ovarian insufficiency was suspected received anterior pituitary extract, oestradiol benzoate, and stilboestrol. Finally, when the cervical erosion did not heal spontaneously after the vaginitis had disappeared, local treatment in the shape of sulphonamides or diathermy was used. Details of administration of drugs are not given.

N. N. Tereshchenko

71. Latent Tuberculosis of the Female Genital Organs. Its Frequency and Importance as a Cause of Sterility in Women. (La tuberculose latente des organes génitaux feminins, sa fréquence et son importance comme cause de stérilité chez la femme.)
By I. HALBRECHT. *Schweiz. med. Wschr.*, 76, 708–709, August 3, 1946. 3 refs.

The author gives the results of investigation of 820 sterile women, all of whom were subjected to diagnostic curettage 2 to 3 days before a menstrual

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period to determine whether ovulation was occurring. Forty-five cases (5.5 per cent) showed histological evidence of tuberculous endometritis. This is in contrast to 5 cases out of a series of 5,516 investigated by Dominguez. In all but 2 cases the normal signs of a secretory phase were found. Forty-three were cases of primary sterility. A further series of 54 sterile women, in whom partial or total occlusion of the tubes had previously been demonstrated, was subjected to curettage, and 18 (33.3 per cent) were found to have tuberculous endometritis. All were free from symptoms of tuberculosis and few had possible tuberculous antecedents. The author concludes that latent genital tuberculosis occurs relatively frequently in women, and particularly in sterile women, that it nearly always leads to eventual blockage of the tubes, that salpingostomy in such cases would be useless and treatment should be rigidly conservative.

[These observations were made on Palestine Jewesses.]

S. S. B. Gilder

See also No. 19.

New growths of the reproductive organs.

72. **Prevention and Treatment of Carcinoma of the Vulva.**
By B. P. WATSON and S. B. GUSBERG. *Amer. J. Obstet. Gynec.*, 52, 179–190, August 1946. 3 figs., 22 refs.

In this paper Watson and Gusberg discuss the prevention and treatment of carcinoma of the vulva, and refer to 30 cases which they have treated. They point out that carcinoma of the vulva is an uncommon disease and occurs at an age when the expectancy of life is not long, and therefore some latitude in the treatment of individual cases is required. They stress the importance of prevention by biopsy excision of any suspicious lesion of the vulva, and excision of the vulva for all cases of leucoplakia causing irritation. In their series of 30 cases the average age was 59 years, the youngest patient being 37. The long period for which symptoms were present before treatment started is noted. This was on an average: pruritus 8 years, lump or growth 1.25 years, and pain 0.69 years. The first symptom was a lump in 18 cases, pruritus in 16 cases, and pain in 6 cases. In 5 of the cases it was not possible to say if the growth was primarily in the vulva or not; 17 cases survived for 2 years, and the cases

traced for longer than this showed that patients dying of recurrence did so within 2 years.

Treatment varied from total vulvectomy with dissection of the glands to lesser surgical procedures with or without irradiation or irradiation alone. The treatment was essentially surgical, irradiation being used for palliation only. (In basal-celled or border-line cases a local wide excision is adequate, and is regarded as the best method of biopsy.) Complete vulvectomy with dissection of the glands of both groins is to be preferred. A one-stage operation is used, and the glands are dissected first. The external ring is incised and fatty tissue removed from the canal. The upper end of Scarpa's triangle is cleaned, but the deep femoral and retroperitoneal glands are not removed. Involvement of the retroperitoneal glands appears to depend on extension of the growth to the vagina, and is well seen in some of the fatal cases. If the vagina is involved all the deep pelvic glands are rapidly involved. Cloquet's gland is removed by most operators, but omission of this stage has not affected the results in the present series. In the discussion which followed, all the speakers agreed that the treatment of carcinoma of the vulva was essentially surgical, and that the 5-year cure rate was in the region of 25 per cent.

L. W. Lausle

73. **Malignancy of the Genitourinary Tract in Children. Report of a Case of Sarcoma of the Vulva.**
By A. C. SERVICE and R. C. DERBYSHIRE. *J. Pediat.*, 29, 228–232, August 1946. 3 figs., 11 refs.

74. **Sarcoma of the Vulva.**
By W. K. DIEHL and J. S. HAUGHT. *Amer. J. Obstet. Gynec.*, 52, 302–310, August 1946. 6 figs., 8 refs.

The literature relating to sarcoma of the vagina is briefly reviewed by the authors. Two cases are described occurring at the University of Maryland amongst 8,589 gynaecological admissions. The first case, a 21-month-old white child, was of the well-known botryoid type. Symptoms of bleeding and vaginal discharge had been present for 3 months before advice was sought. Small polypoid masses were found growing from the right lateral vaginal wall. Microscopically the tissue removed was seen to be myxosarcomatous. The growth was removed, and two 50 mg. radium plaques were applied to the base for 10 hours. Two months later multiple recurrences were present, and radiotherapy totalling

2,072 r units was given. Five mouths later death occurred. Necropsy showed extensive local spread involving all the pelvic organs. There were no distant metastases. In the adult, sarcoma of the vagina is rarely of the botryoid type but is seen either as a mucosal or parietal (submucosal) type. The second case presented is of the adult type in a negress of 40 years. The complaint was of vaginal soreness and slight bleeding on trauma. A walnut-sized tumour covered with a greyish-white exudate was seen half-way up the right antero-lateral vaginal wall. The growth was removed to the level of the surrounding vagina, and 100 mg. radium screened with the equivalent of 3 mm. lead was applied to the surface for 30 hours. Since treatment there has been a gradual regression of the growth without further extension. Commenting on the treatment of vaginal sarcoma, the authors suggest local removal of the growth, possibly by electro-surgery, and application of radium in suitable dosage to the base thereby exposed. Deep *x*-ray therapy is a valuable adjunct. The prognosis in the infantile botryoid type and in the adult forms is uniformly bad on account of the rapidity of extension and tendency to local recurrence.

B. Rickford

75. **Cyst of Skene's Gland.** (Kyste de la glande de Skene.)

By J. LEGAULT. *Un. méd. Can.,* 75, 777–779, July 1946. 1 fig.

The author describes a case of frequency of micturition with dysuria due to a cyst of the gland of Skene in the urethra of a woman of 36. He discusses the differential diagnosis from urethral polyp, urethral prolapse, diverticulum, calculus, and herniation into the urethra of a cystic dilatation of the lower end of the ureter. Treatment by removal of the cyst is extremely simple and satisfactory.

S. S. B. Gilder

76. **Endometriosis: a Surgical Problem.**

By D. MACLEOD. *Brit. J. Surg.,* 34, 109–116, October 1946. 10 figs., 57 refs

77. **Endometriosis in Youth.**

By J. FALLON. *J. Amer. med. Ass.,* 131, 1405–1406, August 24, 1946. 16 refs.

The author reports 9 (4 per cent) of a series of 225 cases of endometriosis as occurring under 20 years of age. This is surprisingly high, as previous reports have always stressed the rarity of this condition in youth. It is suggested that this rarity is only apparent, and that the disease should be considered in the differential diagnosis of abdominal pain as soon as menstruation has been established. There is some evidence that endometriosis tends to develop when menstruation has been uninterrupted by pregnancy for 5 years, so that it might be reasonably looked for at 17 to 19 years. The 9 cases reported here were all verified histologically; if other cases were included in which there was only macroscopic evidence the percentage would have been doubled. From the clinical aspect the cardinal symptom, apart from pain, is increasing dysmenorrhoea, and the discovery of the lesion depends on using an adequate mid-line incision for pelvic exploration when operating for doubtful appendicitis.

A. D. Le Vay

78. **Endometriosis of the Small Intestine.** (Endométriose du gréle.)

L. MICHON and C. OLIVIER. *Presse méd.,* 54, 534–538, August 17, 1946.

The authors describe 2 cases of endometriosis of the small intestine in which the only symptoms were those of intestinal obstruction and the diagnosis was made by the pathologist.

The first patient, a woman aged 33, had recurrent pains in the right iliac fossa over a period of 6 months. Periods were painless and regular. Laparotomy, performed with a view to appendicectomy, revealed a hard mass in the ileum 4 in. (10 cm.) above the ileocaecal valve with peritoneal adhesions around it. End-to-end anastomosis was performed. The patient died on the sixth day of pulmonary embolism. Histologically, endometriosis was found in the longitudinal muscle layer.

The second patient, a woman aged 41, who had suffered from blood-stained diarrhoea for 15 years, was admitted with acute intestinal obstruction. Her emaciation and the absence of other physical signs pointed to a tentative diagnosis of tuberculosis. At laparotomy a tumour some inches above the ileocaecal valve was found. Ileostomy was performed. A later X-ray examination showed a stricture at the rectosigmoid junction. After 3 weeks a second laparotomy revealed easily-separated adhesions round the rectum, with normal ovaries. The ileal tumour was resected and the

patient made an uneventful recovery. Histologically the specimen showed typical endometriosis. In neither case had there been any menstrual disturbances.

S. S. B. Gilder

79. **Endometriosis of the Recto-sigmoid Junction Simulating a Neoplasm.** (Endométriose de la jonction recto-sigmoïdienne ayant simulé un néoplasme.)

By H. GUIAS, J. MINET, and B. DUPERRAT. *Paris méd.*, 36, 430–432, October 5, 1946. 1 fig.

The authors record a case of endometriosis of the recto-sigmoid region simulating carcinoma. Endometriosis of the pelvic colon and recto-sigmoid region is rarely met with, though localization in the pouch of Douglas is fairly common. Diagnosis of intestinal and rectal endometriosis is difficult but important, because if the condition is not recognized the patient may be subjected to unnecessary surgical treatment.

Cuthbert E. Dukes

80. **Differential Diagnosis of Lutein Cysts and Ectopic Pregnancy.** (Quiste luteinico. Su diagnostico diferencial con el embarazo tubario.)

By R. L. MASCIOTTRA and E. P. BAGNATI. *Rev. méd.-quir. Pat. fem.*, 25, 164–172, May 1946. 12 refs.

The differential diagnosis of lutein cyst is often difficult, and many cases are wrongly diagnosed as ectopic pregnancy. Certain laboratory investigations may help to solve the diagnostic problem, as in the case recorded. A patient aged 29 from whom bilateral cysts of the ovaries had been removed 2 years previously had persistent amenorrhoea. Examination revealed pigmentation of the nipples and engorgement of the breasts with some secretion. The uterus was slightly enlarged, with a tender, cystic swelling to the left of the uterus. A Friedman test was negative. Endometrial biopsy showed endometrium of a secretory type, corresponding to the fourth week of the cycle. At laparotomy a lutein cyst of the left ovary was removed. Uterine haemorrhage occurred 24 hours after operation, and normal menstruation 5 weeks later.

Signs of early pregnancy with a swelling in the fornix, as in this case, suggest a diagnosis of ectopic gestation, but these signs also occur with lutein cyst. Differential diagnosis depends on the following. (1) *Examination of endometrium.*— In lutein cyst, the secretory phase is the rule, but

a pseudo-decidual reaction may occur in cases of long-continued action of a corpus luteum on the endometrium, and may lead to confusion with ectopic gestation. (2) *Biological tests for pregnancy.*—These are not always reliable; a negative test is usual with lutein cyst, but sometimes occurs in ectopic pregnancy; a positive test, on the other hand, has been reported in cases of lutein cyst, possibly due to excessive production of pituitary gonadotrophin, because there is diminution in the amount of oestrogen produced and thus enhanced anterior pituitary secretion. (3) *Pregnandiol assay.* This should be carried out in cases where there is doubt; excretion is increased both in ectopic pregnancy and in lutein cyst, but in the latter condition, the increase is much greater. (4) *Exploratory colpotomy.*—The operation is the final test in cases where the diagnosis is in doubt. It is much less traumatizing than laparotomy, and permits thorough exploration of tubes and ovaries. If the diagnosis of lutein cyst is confirmed, nothing further is required. In cases of ectopic pregnancy, if the gynaecologist is accustomed to the technique of vaginal operations, it may be possible to complete the operation by this route. In difficult cases laparotomy is undertaken, but with the diagnosis established.

[This is a sound paper on a subject which often leads to error. Many gynaecologists would not operate for ectopic pregnancy if the biological test was negative and there was no pain; such cases often subside and do not need operation. Posterior colpotomy has never found much favour in Britain, though some gynaecologists, as an alternative, explore the pouch of Douglas with a needle in cases of ectopic pregnancy. Where the operator is familiar with the technique, posterior colpotomy is often a useful procedure.]

Josephine Barnes

81. **Chorionic-Gonadotrophin and Ovarian Tumours.** (Gonadotrophines et tumeurs ovariennes. Gonadotrophinurie dans un cas princeps de dysembryome polyembryonique et chorio-épithéliomateux avec puberté précoce incomplète.)

By M. SORBA. *Gynaecologia*, 122, 53–67, July-August 1946. 2 figs., 56 refs.

The author reports the detailed findings in a case of malignant ovarian teratoma in a child aged 2 years, claiming this to be the youngest case reported in the literature of a teratoma containing

chorionic epithelial tissue. The symptoms were abdominal pain and increasing size of the abdomen for some months. There had been some white mucoid discharge vaginally but no periods. Though the breasts were palpably enlarged there was no growth of pubic hair. Abdominal examination showed a large tumour reaching to the umbilicus which, on laparotomy, proved to be an ovarian tumour arising on the right side with spread to the right iliac and aortic glands. There was a small similar tumour in the left ovary. The uterus was enlarged. The right ovary was removed and the tumour in the left was shelled out. The tumour weighed 1,420 g. and microscopical examination showed multiple tissues which included chorionic epithelium.

Having previously been interested in hormonic assays in cases of testicular tumour and having been struck by the easier interpretation of similar assays in the female before puberty, the author followed this patient up by gonadotrophic estimations. Two days after operation the Friedman test was positive in 30 and 50 ml. and negative in 5 and 10 ml. of urine. The reaction became negative within 3 months of operation. The child died from metastases 8 months later.

Such teratomata are rare, Miller (Henke-Lubarsch: *Handbuch der pathologischen Anatomie*, 1937, Teil VII, Bd. 3) recording only 20. The author could find 9 below the age of puberty which have been reported. He also reviews the literature on gonadotrophic excretion in cases of ovarian tumours and comments on the variation in findings of different authorities.

R. K. Bowes

82. **The Clinical Treatment of Ovarian Carcinomata.** (Beitrag zur Klinik und Therapie der Ovarialcarcinome.)
By K. ABT. *Gynaecologia*, 122, 75–109, July–August, 1946. 1 fig.

Two 10-year series of cases of ovarian carcinoma are reviewed here, one series for 1921–33 at the women's diseases clinic at Zürich, the other being for 1928–38 at a similar clinic at Basle. There were 105 cases at Basle out of 13,637 gynaecological patients, of whom 768 had genital carcinoma. At Zürich the corresponding figures were 79 cases out of 10,931 admissions and 658 cancer cases. The proportion of malignant to benign ovarian neoplasms was 18.7 per cent at Basle and 18.8 per cent at Zürich. The greatest incidence relative to 5-year age periods was between 35 and 65, this span having 82 per cent of the cases. There appeared to be no particular relation to previous parity. Of patients with primary carcinoma or cancer developing in a simple tumour 34 per cent were sterile. Only 23 per cent of patients with secondary ovarian carcinoma were sterile. Between 20 per cent and 23 per cent of the patients had a familial history of cancer (cf., 16 per cent in non-cancerous affections of the same age period 40–60 years); 31 per cent of the tumours were primary carcinomata, 57 per cent appeared to have developed in previously existing benign tumours, and 12 per cent were metastatic in origin. Most histological types occurred in the primary series, the previous benign lesions being cystadenoma 57, dermoid 2, and teratoma 1. The author refers to the well-known difficulty of classification of some of the papilliferous growths. Of the metastatic tumours 9 had their source in the stomach, 2 in the breast, and 2 in the gall-bladder.

Analysis of the cases not of metastatic origin showed clinically 3 groups. Group 1 contained those in which the growth macroscopically was confined to the ovary itself. In Group 2, the growth had extended beyond the ovary but complete removal was possible at operation, while in Group 3 the extension of the growth made complete removal impossible. 67–77 per cent of patients had growths at operation of group 2 or 3—i.e., the prognosis is unfavourable in this high proportion of patients. The right ovary was the site of tumour in 33.3 per cent, the left in 27.6 per cent and both ovaries in 23.8 per cent. Most were large tumours (47.6 per cent) and 77 per cent had metastatic spread to the peritoneum, pouch of Douglas and pleura. Symptomatically 60 per cent of patients gave a history shorter than 3 months, and about the same proportion gave a history of abdominal pain as the main symptom. Other symptoms were constipation and bowel disorders (40 per cent), urinary symptoms (17 per cent), and genital bleeding (28.6 per cent). The bleeding from the genital tract was not always due to the carcinoma; 6 had metastatic deposits in the uterus and vagina, and other lesions found were fibroids and polyps. The author was not as impressed as some have been by the association of bleeding with ovarian carcinoma and this is reasonable as many tumours do not contain endocrines. No feminizing symptoms occurred. In addition,

ascites was present in 63 per cent and pleural fluid in 2 per cent. The blood sedimentation rate was not altered sufficiently frequently to consider it of value in diagnosis. Loss of weight was a very significant sign.

Kenneth Bowes

Operations.

83. **Post-Operative Activity and Resumption of Normal Movement. Their Influence on Embolism and Thrombosis.**

By G. FitzGibbon. *Brit. med. J.*, 2, 413–416, September 21, 1946. 6 figs., 6 refs.

The recent tendency to advocate an increase in activity after operation as a prophylactic against complications such as embolus has led the author to develop a method of post-operative treatment which aims at the restoration of natural movements, the adoption of restful positions, and thus the restoration of the activity of the trunk muscles.

The abdominal wound, including skin, is closed with continuous sutures of plain catgut. No tension sutures are inserted. Two strips of 1-in. (2.5 cm.) strapping are laid across the incision, and 3 or 4 layers of gauze cover the line of suture. The whole is covered by a sheet of plaster 5 × 7 in. (12.5 × 17.5 cm.), held in place by a band of 3-in. (7.5 cm.) strapping along the top. The dressing is not moved until the fifth to seventh morning. When the abdomen is drained additional gauze is placed over the tube and kept in place with strapping and a " T " bandage. After vaginal operations no tampon or drain is inserted; the vulva is covered by a pad. Tension sutures and clips are avoided as they cause pain. A binder is used for 12 hours to prevent the strapping being displaced. The patient is put on the trolley in the same position as she will be in bed—in complete flexion on her side. She is lifted into bed lying on one side, so that the body tends to fall into a prone position. The head is flexed forward, resting on a pillow, with the mouth slightly dependent. When deep anaesthesia passes off the patient will tend to adopt a twisted position, resulting in painful stiff muscles—a potent factor in the subsequent disinclination to move. A nurse should assist her into the opposite flexed position. This proceeding may have to be repeated until she is sufficiently awake.

On the first morning, for short periods, the patient sits up in bed in a comfortable relaxed posi-

tion, moves up on her pillows, or props herself on her elbows. On the second day she sits up in bed, so as to allow her whole spine to flex, her shoulders to `drop, and to sit easily balanced for a few minutes. Once complete flexion of the spine has been obtained the guarding of the muscles will pass off. From the third day the patient freely moves in bed, and gets out to urinate and defaecate. At intervals through the fourth or fifth day she sits up for half an hour. During the second week patients walk about the ward. They go to the lavatory and have baths from the ninth or tenth day. The essence of management in early convalescence is to obtain active muscle exercise of the whole body all through the day, but never to continue beyond the least feeling of fatigue.

Post-operative sedatives should not be given until there is definite pain in the wound. They may be repeated through the first 2 or 3 nights, but omitted in the daytime. In 7 to 9 hours, and at regular intervals afterwards, the patient is asked to pass urine on the bed-pan or, preferably, out of bed. If this fails, a catheter is passed. One ounce (28.4 ml.) of liquid paraffin is given on the second and third days, and the patient tries to have a bowel action on the night-chair after breakfast each day. If necessary a small enema or a mild laxative may be given.

In the past 25 years, among over 700 hysterectomies, the author has never had a death from, nor even symptoms suggestive of, pulmonary embolus after operation. In the only 3 postmortem specimens he recollects, the clot had formed in the pulmonary artery, and the author bases his treatment on the belief that this is what occurs in practically all fatal cases. Treatment is by prevention, and is effected by promoting circulation by active movement.

The treatment of venous thrombosis is based on the same views. Thrombophlebitis being due to infection, treatment is directed towards the cause. When the acute stage is passed movement should be encouraged. Earlier recovery is promoted by allowing the patient to get up and use the limb as soon as the primary pain has passed. Thrombosed veins are unimportant as there is no tendency to embolus. The limb is ignored beyond placing a cage over it, or putting a pad over a painful surface vein.

There are absolutely no contra-indications to

active movement. The one essential demanded in all operations is complete haemostasis.

W. R. Forrester Wood

81. **The Manchester Operation, with Special Reference to Parturition and Complete Prolapse. A Report of 206 Cases.**
By C. A. GORDON. *Amer. J. Obstet. Gynec.*, 52, 228–236, August 1946. 41 refs.

Gordon discusses the Manchester operation with special reference to parturition and complete prolapse and reviews a number of cases. The necessity for shortening the transverse ligaments in operations for prolapse is now generally agreed, and the Manchester operation is based on this principle. Genital prolapse is a comprehensive term including many varieties of weakness, and it is clear that one operation will not cure all cases. For example, the Manchester operation will not cure enterocele and rectocele. His own experience of the Manchester operation makes it difficult to agree with the common view that this operation should not be used in patients likely to become pregnant or in cases of complete prolapse. Before 1932 many operations were employed in the U.S.A. for prolapse, but since that time the Manchester operation has become increasingly popular. In the 10-year period 1934–43, 236 operations for prolapse were carried out at St. Catherine's Hospital, Brooklyn, nearly all under local analgesia. The Manchester operation was used in 206 cases, vaginal hysterectomy in 21, Le Fort's operation in 2, and the interposition operation in 7 cases. Thirty-six of these patients were under 40 years of age and liable to become pregnant, and 10 patients had become pregnant. In 5 the course of pregnancy was unknown, and in the other 5 one was delivered with an episiotomy only, 3 with forceps, and 1 required Caesarean section for a rigid cervix.

A review of the literature shows that amputation of the cervix may cause abortion and rigidity of the cervix in labour, and is not a good operation for women in the reproductive period, whether by itself or as part of the Manchester operation. The combined operation shows a high incidence of recurrence after parturition. Results following parturition after the Manchester operation are reviewed, but it is not certain if in these cases the cervix was removed or not. The nature of delivery and recurrence appears to vary considerably with

different writers. In the above series there were 89 cases of complete prolapse, and in the personal series of 26 cases there were no recurrences.

L. W. Lauste

85. **The Sterilization of Females at Auschwitz Concentration Camp.** (La stérilisation féminine au camp d'Auschwitz.)
By P. FUNCK-BRENTANO. *Méd. français, Paris*, 6, 257, September 10–25, 1946.

The author's interest in this subject was roused by the examination at his clinic of a young Polish woman who had been submitted to an intra-uterine injection of a caustic substance at Auschwitz Concentration Camp. A former pupil who was interned there for 2¼ years gave him further details, and he also summarizes facts given by a Russian Commission which had deportee doctors at Auschwitz as members. These included Dr. Limousin, a professor of the medical faculty of Clermont-Ferrand. One block of the camp hospital was reserved for experiments on women. The experiments included the testing of various substances for contrast media for radiography of the genital organs, methods of sterilization, and studies on the ovaries removed following radiological sterilization. Prof. Glauber of Breslau was the surgeon in charge. It is clear that hundreds of cases were dealt with. The patient examined by the author had had an intra-uterine injection of some caustic followed by much pain and pyrexia. When examined the cavity of the uterus was found to be small, the left tube was occluded at the uterine end and the right one was blocked a short distance along. Such experiments were possibly made to provide methods of extinguishing populations deemed unsuitable by the Reich and also to test endocrine preparations.

R. K. Bowes

Urology.

86. **Prostatism in Women.**
By S. R. HOOVER. *Urol. cutan. Rev.*, 50, 326–328, June 1946. 2 refs.

The title of this paper, as the author points out, is somewhat misleading. He reviews 45 cases in women whose chief complaint was frequency and urgency of micturition, associated with pain and burning and occasionally haematuria; there was also, in 1 or two cases, difficulty in emptying the bladder. All these complaints were aggravated

when the patient was standing, and a limited degree of relief was obtained on lying down. Nocturia was seldom reported, and apart from occasional pus cells and commonly alkaline urine, nothing abnormal was found on analysis of the urine; in fact, in general, the urine was clear and sparkling.

On cystoscopy the mucosa of the posterior urethra presented a " moth-eaten " appearance in the first 1 cm., and there were 1 to 3 longitudinal fissures extending over the vesical neck to the bladder-mucosa. Between these fissures were sharp elevations, tending to bleed from their summits. Just inside the internal urethral orifice of the bladder-the mucosa was hypertrophied sufficiently to form a definite ridge or bar across the posterior aspect of the orifice. He considers that the symptoms were due to this ridge or bar. Stricture of the urethra was not encountered in any case. The normal angle formed by the bladder and urethra was frequently altered by 45 to 90 degrees, the internal orifice being anterior to the external orifice with the patient in the upright position. The residual urine varied from 0 to 15 ml.

All cases were treated by electro-coagulation of the mucosa of the posterior urethra with removal of the elevated bladder mucosa, when necessary, with the cutting current. The urethral mucosa was destroyed down to the connective tissue, care being taken not to damage the sphincter. Using a 24 French McCarthy electrome, three or four small pieces were removed from the vesical neck. The microscopic report on these sections is summarized as follows : thickening of the mucosa; oedema; varicosity of the blood vessels; lymphocytic infiltration; fibrosis.

The author states that the degree of relief has varied from immediate and complete to delayed and partial, but in no case did the patient feel that the operation had not been worth while

[It is significant that all the 45 cases reported were of private patients, and no glandular structure was found in the tissue removed.]

A. W. Badenoch

See also No. 2.

Radiography as an Aid to Dose-Control in the Radium Treatment of the Cervix

BY

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RADIOTHERAPY of cancer demands that the whole of the tumour-bearing tissue be irradiated with an adequate dose. When radium is being applied locally to the growth, notice should be taken of the fact that the intensity of radiation falls off very rapidly with increase in distance from each individual component of the radium assembly. The radium must, therefore, be arranged with precision if an adequate irradiation of the outlying parts of the tumour is to be achieved without causing damage to the tissues near the radium.

The mechanical flexibility of the radium applicators used in the " Stockholm " type of treatment of cancer of the cervix allows easy adjustment to the configuration of any individual case; but at the same time this variation of the arrangement from case to case also produces considerable variations in the distribution of the physical dose. It is, therefore, desirable in the control of the treatment to ascertain in each case the exact arrangement of the radium, and to assess the distribution of radiation.

The following presents the data of some typical cases from a series investigated at St. Mary's Hospital during 1946.

The investigation of the physical dose of radium insertions is based on the use of charts showing the distribution of radiation around the individual sources in use, i.e.: Intrauterine tube containing 2 × 20 mg. Vaginal boxes containing 5 × 5 mg. each.

These charts consist of isodoses, lines linking the points exposed to an equal intensity of radiation from the source. The intensity is expressed in roentgens per hour (r/hr.).

Two points emerge on examining these charts (Fig. 1):

(1) The very rapid decrease of intensity with an increase of the distance from the source, e.g.: Intensity 1 cm. from the vaginal box, 150 r/hr. Intensity 2 cm. from the vaginal box, 40 r/hr.

(2) for distances greater than about 2.5 cm. the isodoses closely follow circles which are centred on the centre of the box. This means that for such distances the

dose is mainly governed by the distance from the centre of the box and is largely independent of any tilt or rotation of the box through its centre.

Fig. 2 represents an arrangement of the radium which has been described as ideal. The scale drawing shows that the vaginal vault must be stretchable to a total width of 7 cm. for this arrangement to be carried out. In practice, the ideal arrangement is very rarely achieved.

The estimation of the dose delivered is obtained by a simple summation of the doses contributed by the individual sources. The total dose (continuous line in the graph) is expressed in r/hr. and the dose in r. is calculated for 3×22 hours, which is the standard time for this arrangement. The dose is estimated along two lines extending laterally from the uterine canal at levels 1 cm. and 2.5 cm. above the level of the external os (lines b and a respectively in Fig 2). This permits a better visualization of the dose distribution along the usual path of extension of the growth than if the dose assessment were carried out for 1 or 2 selected points only. The upper plane lies near point "A" of Tod which is described as being situated 2 cm. above the vaginal vault and 2 cm. lateral to midline.

In the Stockholm type of treatment by intermittent application it is reckoned that a total of 6,600 r. given in 3 insertions represents an adequate dose. A dose smaller than 4,500 r. must be regarded as insufficient. The position of these dose-levels in the ideal arrangement is indicated in Fig. 2 and it is seen that the dose falls below 6,600 r. at distances greater than 4 cm. from the midline in the lower plane. The effective reach in this arrangement, therefore, is up to 4 cm. from the midline in the lower plane and only 1.5 cm. from the midline in the upper plane. In these circumstances the tissues 0.5 cm. beyond

the wall of the lateral fornix receive a dose of between 10,000 and 14,500 r.

Insufficient width of the vaginal vault or the presence of bulky tumour tissue often prevents the radium application according to the ideal scheme and this arrangement was, therefore, not seen in any of the cases under review.

As the ideal arrangement can rarely be applied it becomes necessary to ascertain the position of the radium in each individual insertion in order to assess the dose given and to guard against a misplacement of the radium. This can be done most conviently by the following radiographic methods.

(a) An antero-posterior and a lateral film. These are difficult to interpret because of the overlapping of dense shadows and because of the magnification-distortion inherent in the method.

(b) Stereoscopic antero-posterior films. These give a very good general survey of the position of the containers but do not permit an accurate measurement of dimensions unless a mensuration stereoscope is used.

(c) In this series a combination of (a) and (b) is used. For a scale drawing of the insertion in the coronal plane the dimensions of the central antero-posterior film are reduced to a natural size by the following formula:—

True dimension = measured dimension

$$\times \frac{\text{Total stereo tube-shift (T.T.S.)}}{\text{T.T.S. plus measured image-shift}}$$

An exaggerated total tube-shift (20 cm.) is employed so that the image-shift on the films is easily measurable. Films thus obtained still permit stereoscopic visualization as an aid. If wanted, an actual model-reconstruction of the implant can be made from the shift-films by means of foreign-body localization methods.

A fairly common arrangement is seen

in Fig. 3. The dose-data of an insertion of this type are given in Fig. 4. This type of insertion requires a total vaginal width of 5 cm. but the whole implant is much less efficient than the ideal type because of the crowding of the radium and the lower position of the centres of the lateral boxes. The fall off of the dose in the periphery is more rapid than in the ideal version. The effective reach as represented by the 6,600 r. dose level is reduced from 4 cm. to 2.75 cm. in the lower plane in spite of an increase of the total time to 3 times 24 hours. The zone of effective irradiation in the upper plane is very little different from that in the ideal arrangement. This increase in the insertion time causes the normal tissues near the applicators to receive a correspondingly higher dose. The estimated dose at a point $\frac{1}{2}$ cm. beyond the wall of the lateral fornix is now 16,500 r. as against a maximum of 14,500 r. in the ideal case. This is almost as high a dose as normal tissues can stand.

An alternative arrangement for a vaginal width similar to that in the foregoing case is presented in Fig. 5. The dose assessment of an insertion of this type is given in Fig. 6. The total amount of radium is reduced by the elimination of the centre' box. This allows the remaining boxes to be positioned in a more satisfactory manner. The time of insertion, however, is increased to 3 × 28 hours. Although the effective reach is similar to that in the foregoing case there is a greater safety factor in this arrangement. This is seen by the fact that the normal tissues at a point $\frac{1}{2}$ cm. beyond the wall of the lateral fornix receive a total dose of 14,000 r. as against 16,500 r. in the position illustrated in Fig. 4.

Another type of insertion is seen in Fig. 8, and the physical dose for 3 insertions of this type of 24 hours each is represented in Fig. 7.

The dose at a point $\frac{1}{2}$ cm. beyond the wall of the lateral fornix is 15,000 r. The zone of effective irradiation extends to 3 cm. beyond the midline along the lower plane.

This type of insertion is preferable to both the previous ones but it requires 0.8 cm. additional space for the reception of the vertically positioned centre box. It is difficult to keep this vertical box in position and to keep the rectum packed well away from it. The use of a cylindrical applicator containing 5 mg. tubes instead of the vertically placed centre box would represent a mechanical advantage.

The type or arrangement often differs in successive insertions in the same case, especially as there is a tendency for the vaginal vault to contract in the interval between the insertions. Figs. 8, 9 and 10 show 3 consecutive insertions in a case and the corresponding dose charts are given in Figs. 8a, 9a, and 10a. It can be seen that the first insertion was the most satisfactory, having an effective reach of nearly 3 cm. on the left side. The uterine-tilt away from the right reduced the effective reach on the right to 2.5 cm. (Fig. 8a). It was not possible to place the radium in the same position during the next 2 insertions on account of contraction of the vaginal vault, and it can be seen from the charts (Figs. 9a and 10a) that the effective reach of the last 2 insertions is reduced by nearly 1 cm. on the left and by $\frac{1}{2}$ cm. on the right as compared with the first insertion (Fig. 8a). The total dose from all 3 insertions is given in Fig. 11 which shows that an effective reach of the whole treatment is 2.4 cm. to the left and 2.3 cm. to the right.

Sometimes the radium insertion is grossly asymmetrical because of distortion of the pelvic structure due to the growth. A case of this type is illustrated in Fig. 12. The corresponding dose-data are given in Fig. 13 and Fig. 13a. Here the infiltrated

and shortened left parametrium has pulled the top of the vagina and the lower end of the uterus over towards the left lateral pelvic wall. The structures are not only displaced but also angulated. The lateral angulation between uterus and vagina was observed in all 3 insertions.

At first sight the deviation of the radium towards the side of the known parametrial spread is welcome, as it suggests an increased irradiation of that region. An analysis of the physical dose, however, shows (Figs. 13 and 13a) that owing to the lateral tilt of the uterus it is the *right* paracervical region which is cross-fired by the radium in the uterus and by the right vaginal box. It is for this reason that the high dose area, although displaced as a whole to the left, extends for 3.5 cm. to the right from the external os but only for 2 cm. to the left of the external os. The area of the left parametrial spread in this case is, therefore, not adequately irradiated.

Radiographic control of radium insertions will also demonstrate the presence and the degree of retroversion of the uterus. The recognition of this condition is important, as the proximity of the intrauterine radium to the rectal wall in retroversions is one of the causes of irradiation damage to the rectum. The degree of retroversion may not be constant. This is illustrated in Figs. 14 and 15, showing the radium arrangement of the first and third insertion in the same patient.

Frank malpositions of the radium are obvious in the radiographs and the lateral film is especially valuable in showing at a glance whether the boxes are retained well up in the fornices (Fig. 16) or whether they have slipped down into the vagina (Fig. 17).

An estimation of the dose delivered by the radium taken together with the clinical extent of the growth will show whether or not the treatment has been physically adequate. Additional irradiation seems indicated where either the tumour is known to extend outside the effectively irradiated volume or where such an extension must be suspected because of the anaplastic nature of the tumour.

It is clear from the foregoing analyses that the Stockholm method can rarely be relied upon to reach tumour tissue situated further than 3 cm. on either side of the midline, so that nearly all Stage II and all Stage III cases need supplementary treatment on physical grounds alone.

Supplementary treatment is usually given by X-radiation and has to be planned for each case so that no undesirable additional irradiation is given to the area already effectively treated by the radium irradiation. It is possible to plan the application of the supplementary X-radiation in such a way that the X-ray dose increases progressively as the radium-dose decreases from the centre of the pelvis towards the lateral pelvic wall. Fig. 18 illustrates this method as applied to an average case. This shows that 6 fields are used and that a pelvic dose of 30 r. in the midline, rising to 90 r. at the pelvic wall is given for each 100 r. applied to each of the 6 fields.

The quantitative assessment of the combined radium and X-ray treatment is difficult in this instance because the *optimum physical dose of the radium treatment is 6,600 r. given in 3 insertions,* whereas the *optimum dose for pelvic irradiation of this type with X-rays seems to be in the order of 2,000 r.* given over 4 to $4\frac{1}{2}$ weeks. The roentgen can here no longer be regarded as the common denominator, and it is suggested that the estimation of the combined dose is expressed as percentage of the optimum. Fig. 19 shows the distribution of both the radium and the X-ray dose expressed in these terms. The chart illustrates that the optimum level of irradiation is maintained throughout the

whole width of the pelvis by either radium or X-ray treatment and it shows how the X-ray treatment can take over where the radium dose becomes inefficient. Thus at the upper plane the radium dose falls below optimum level at 1.75 cm. from midline but at the same point the X-ray dose enters the optimum range and this is sustained right out to the lateral pelvic wall.

ACKNOWLEDGMENTS.

My grateful thanks are due to Dr. H. Courtney Gage for his constant help and advice in carrying out this investigation.

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Tod, M. C., and Meredith, W. J. (1938): *Brit. J. Radiol.,* 11, 869.

FIG. I.
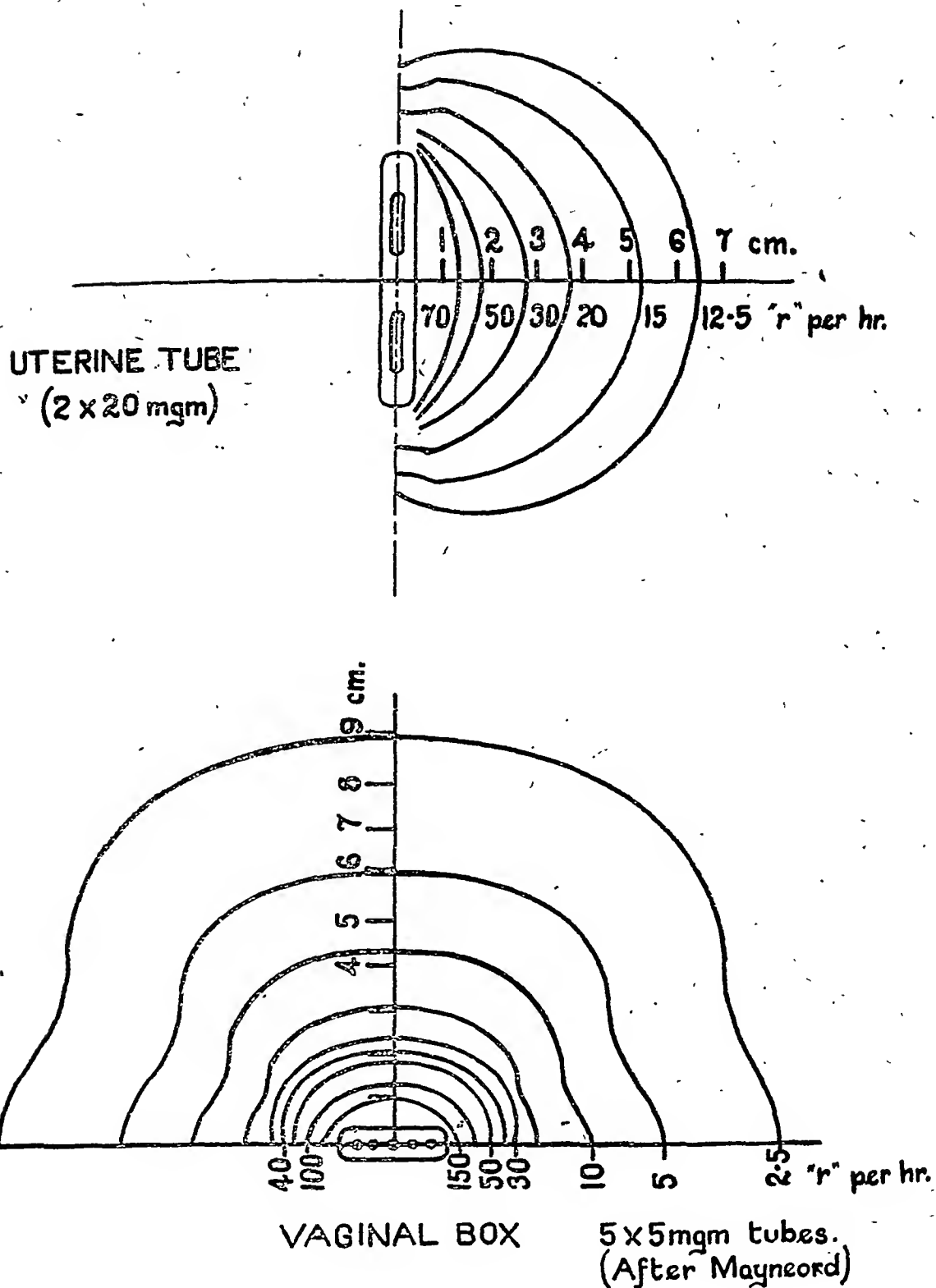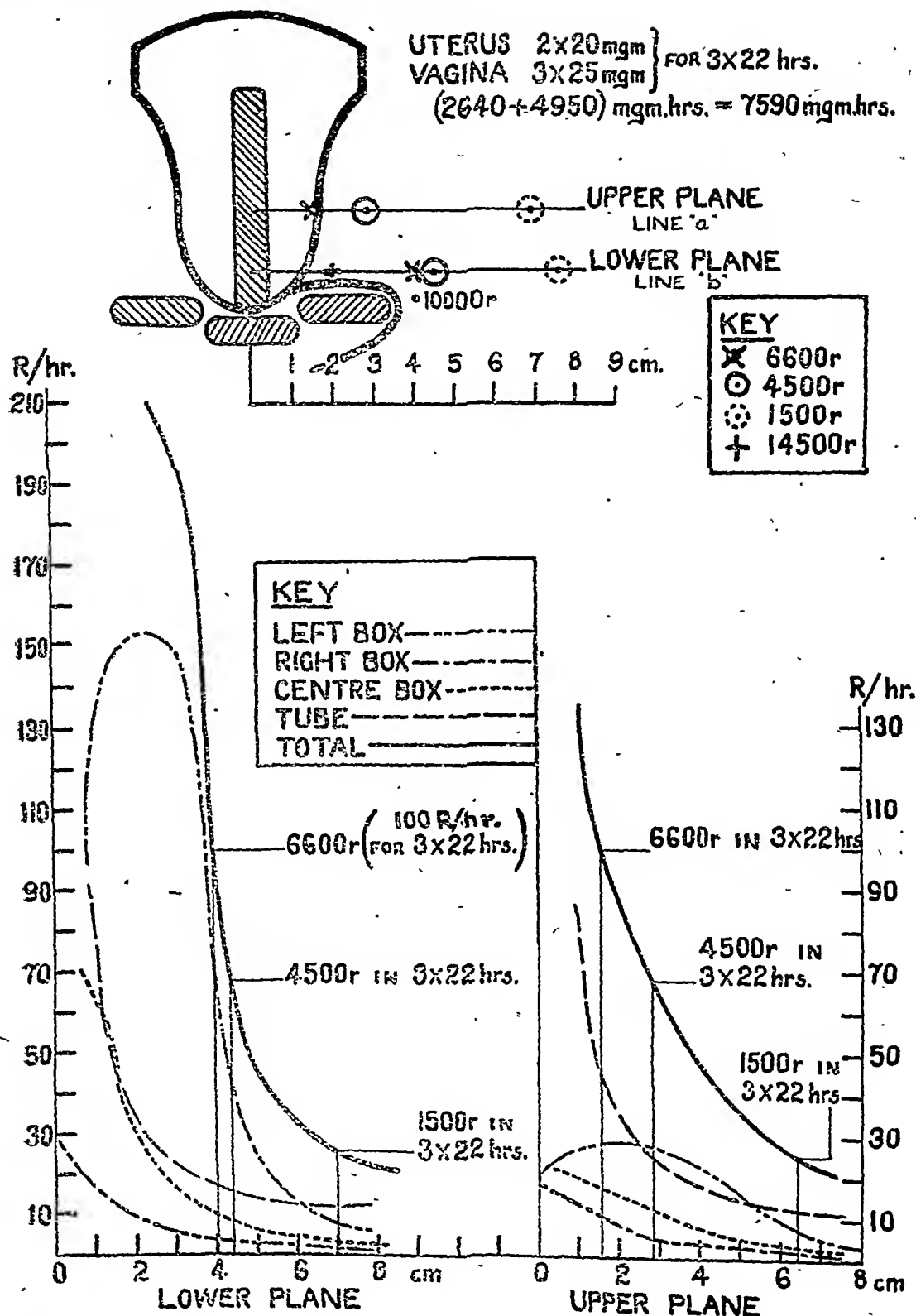
FIG. 2.
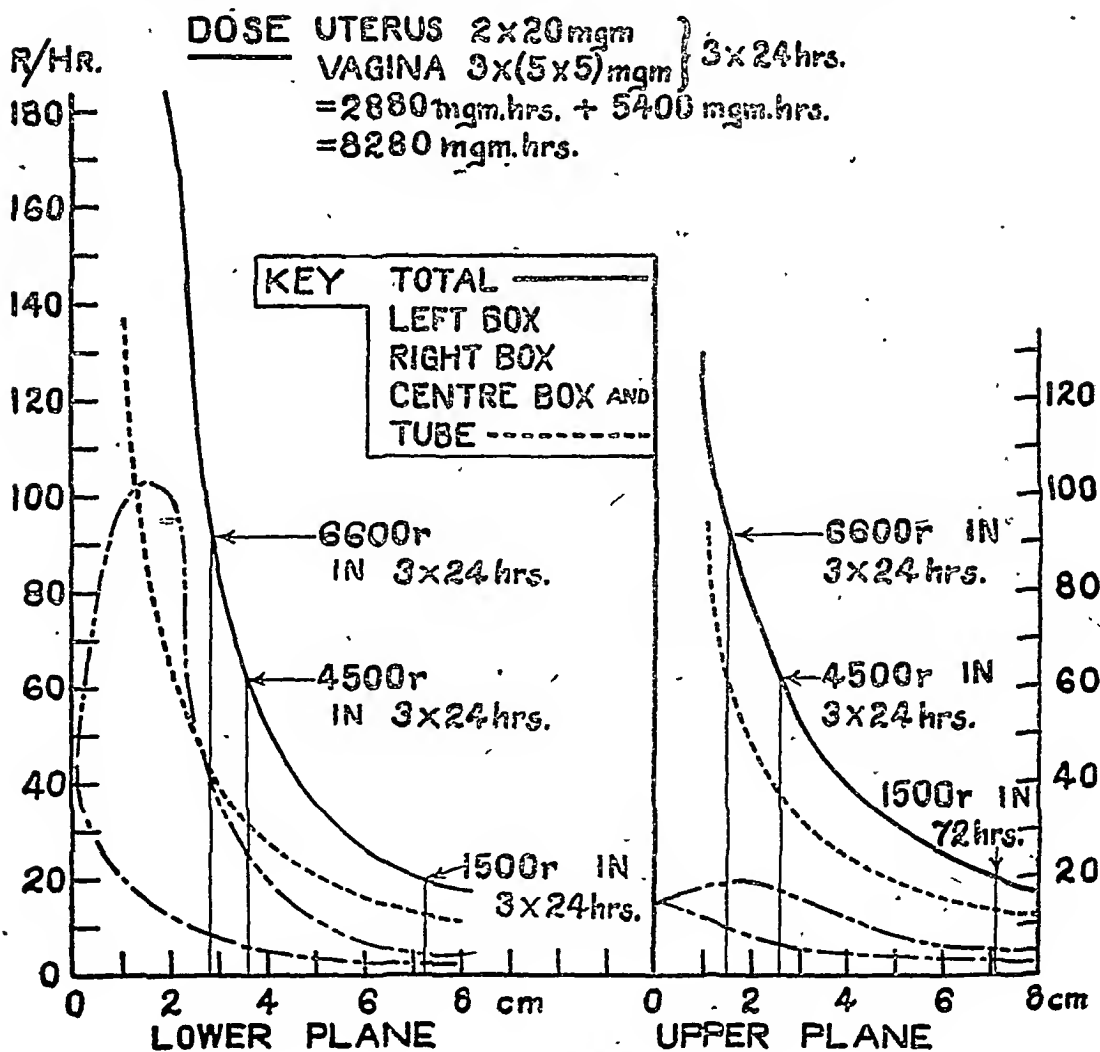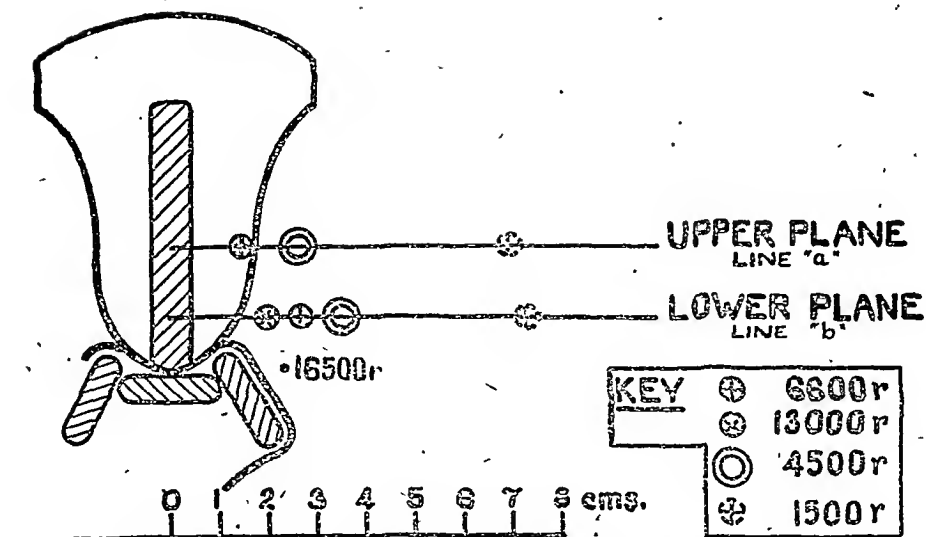
FIG. 4.

FIG. 3.

M.H.E.H.

FIG. 5.
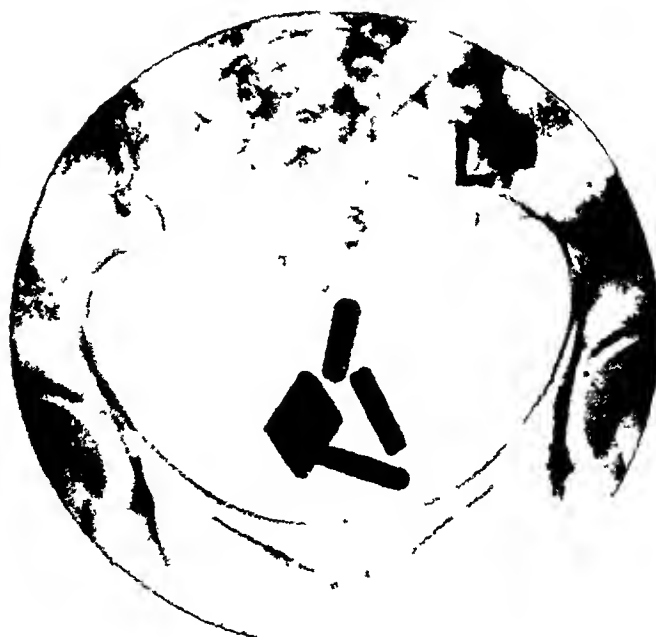
Fig 8.

Fig 9

M.H E H.

FIG. 10

FIG. 12.

M H I .H.
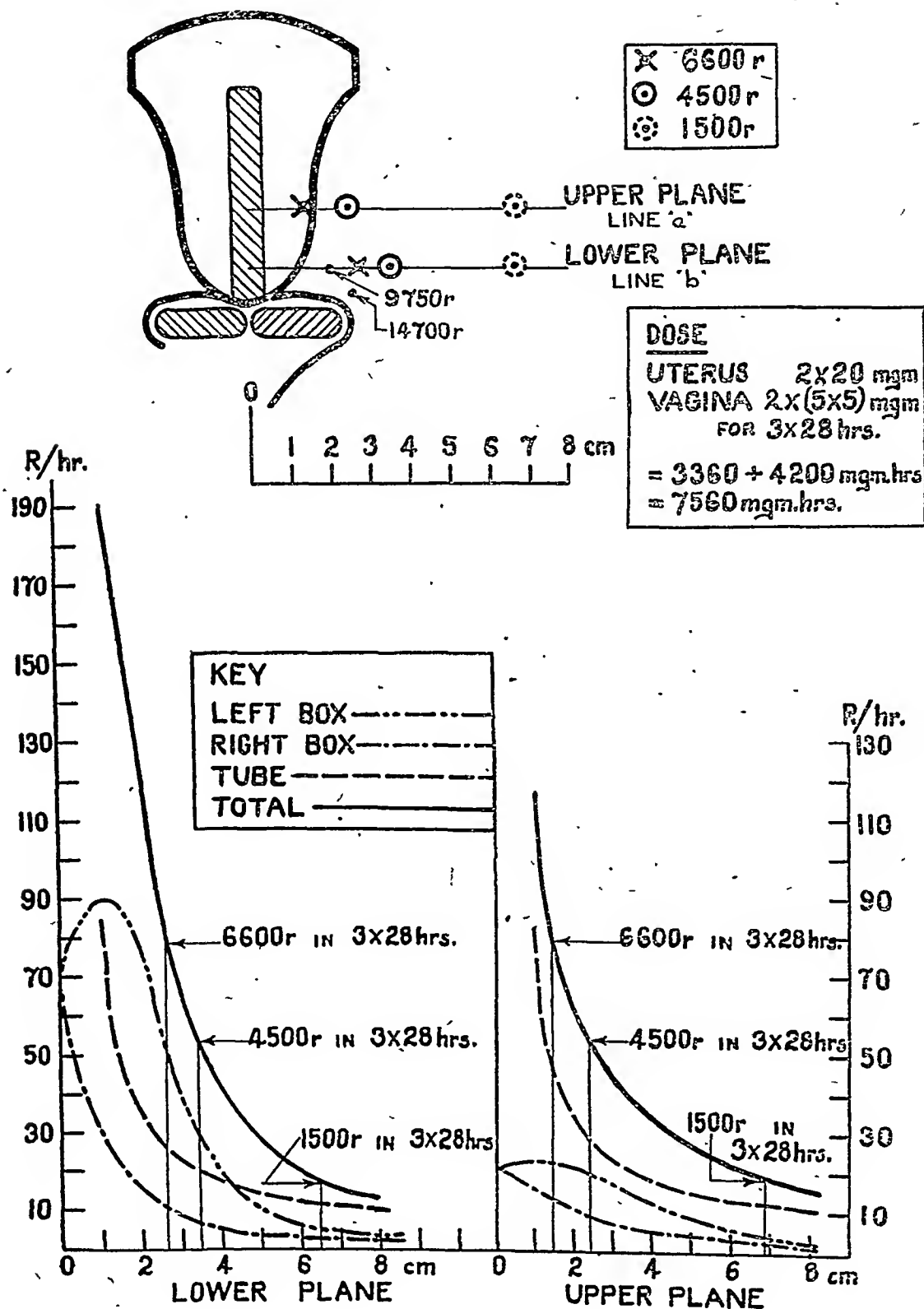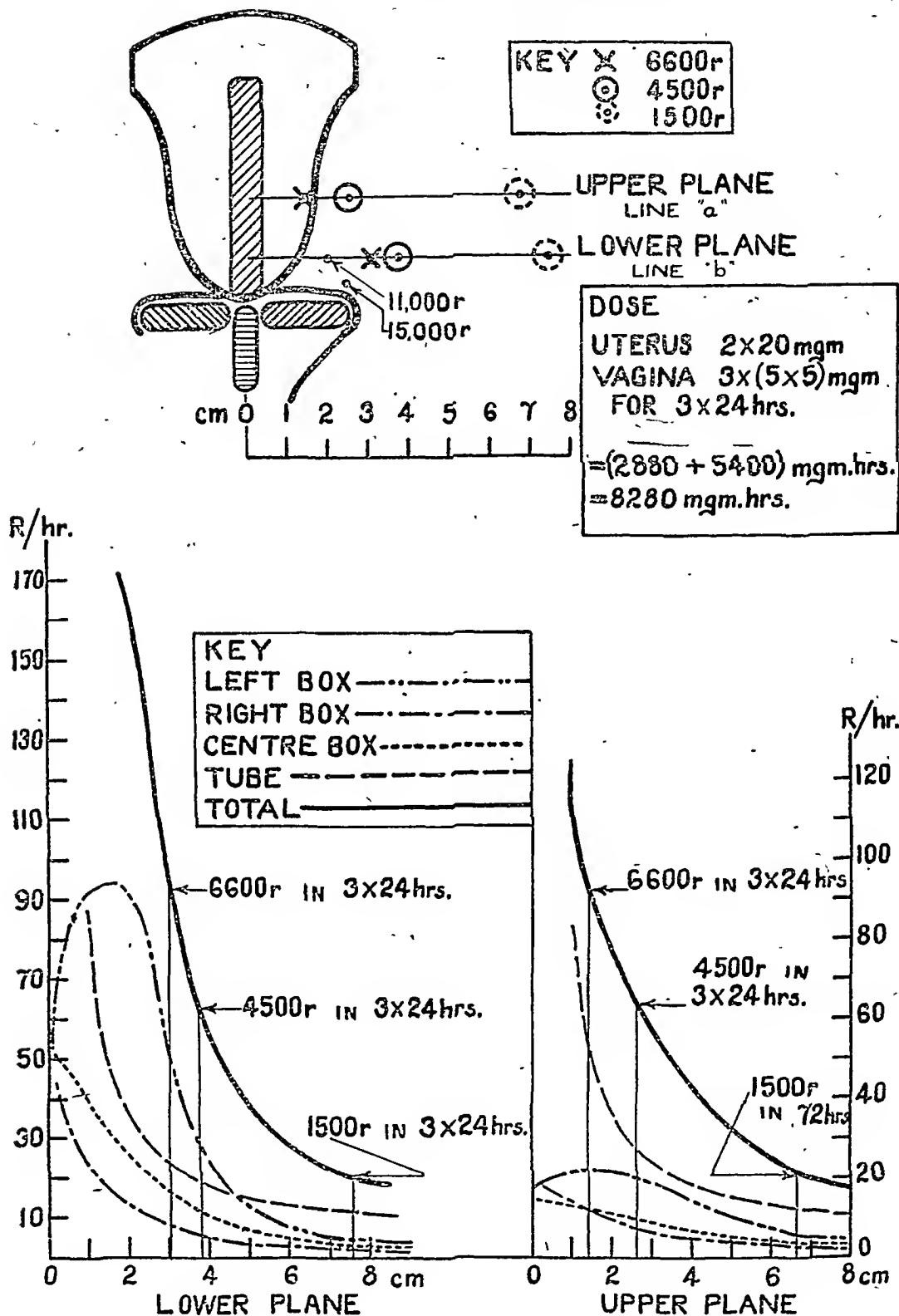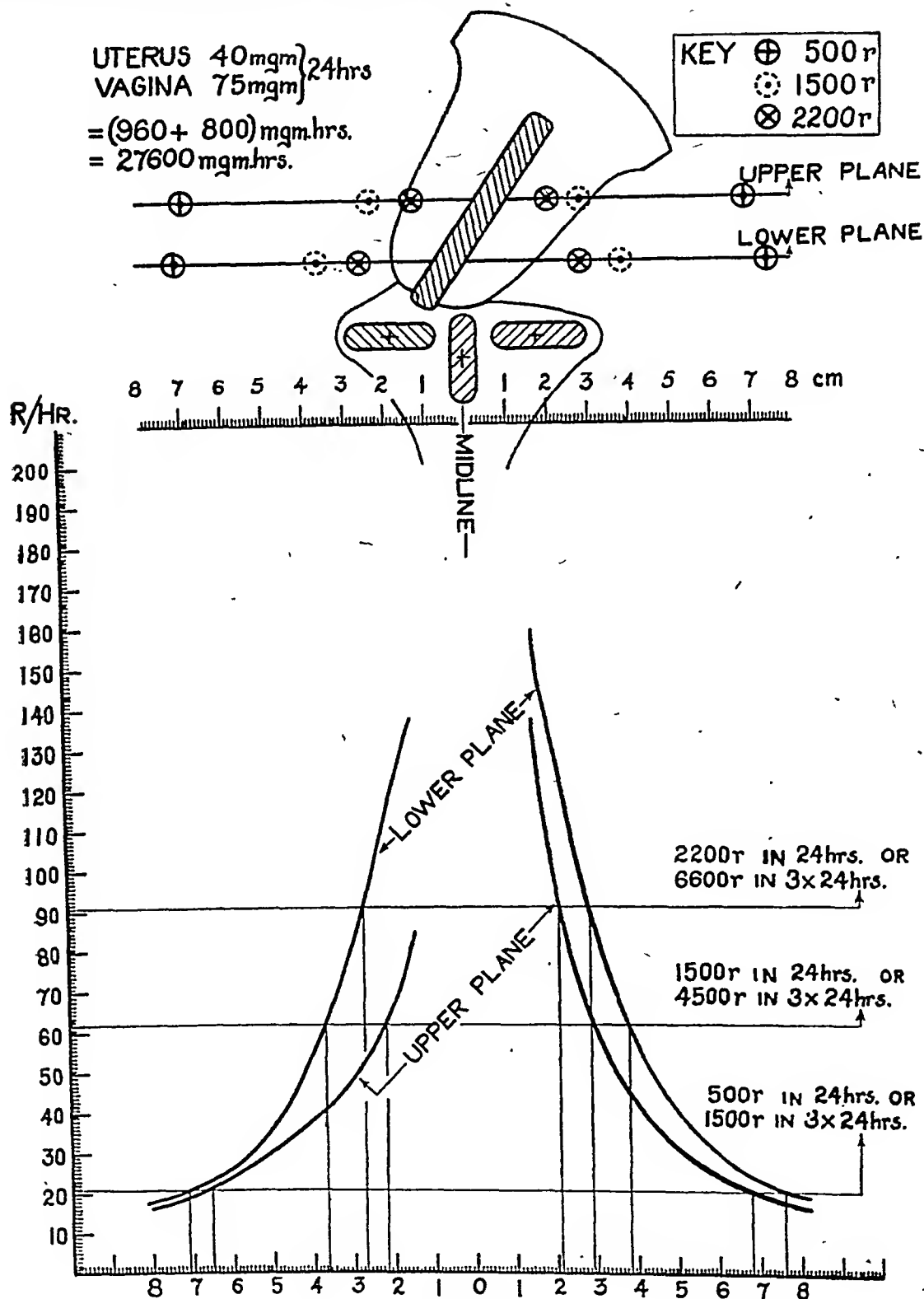
FIG. 14.

FIG. 15.

FIG. 6.

FIG. 7.

FIG. 8a

FIG. 9a

KEY ⊗ 2200r
⊙ 1500r
⊕ 500r

2200r IN 24hrs.
6600r IN 3×24hrs.

1500r IN 24hrs.
4500r IN 3×24hrs.

500r IN 24hrs

FIG. 10a

KEY ◌ 1500r
     ⊙ 4500r
     ✕ 6600r

TOTAL DOSE
3×24 hrs.
8280 mgm. hrs.

MIDLINE

cm 8 7 6 5 4 3 2   0   2 3 4 5 6 7 8 cm

TOTAL FOR 3 INSERTIONS

R/HR. (AVERAGE)

6600r IN 3×24hrs.

4500r IN
3×24 hrs.

1500r IN
72 hrs.

FIG. II.

KEY ⊙ 1500r
⊙ 4500r
✕ 6600r

UPPER PLANE

LOWER PLANE

8 7 6 5 4 3 2 0 4 5 6 7 8 cm

MIDLINE

DOSE

UTERUS 2680 mgm.hrs.
= 2×20mgm FOR 3×24hrs.

VAGINA 5400 mgm.hrs.
= 3×(5×5)mgm FOR 3×24hrs.

TOTAL 8280 mgm.hrs.

R/HR.

KEY
LEFT BOX —·—·—
RIGHT BOX —··—··—
CENTRE BOX ············
TUBE. —— ——
TOTAL ————

6600r IN
3×24hrs.

4500r IN
3×24hrs.

1500r IN
3×24hrs.

cm 8 7 6 5 4 3 2 1 0 1 2 3 4 5 6 7 8 cm

RT. UPPER PLANE LT.
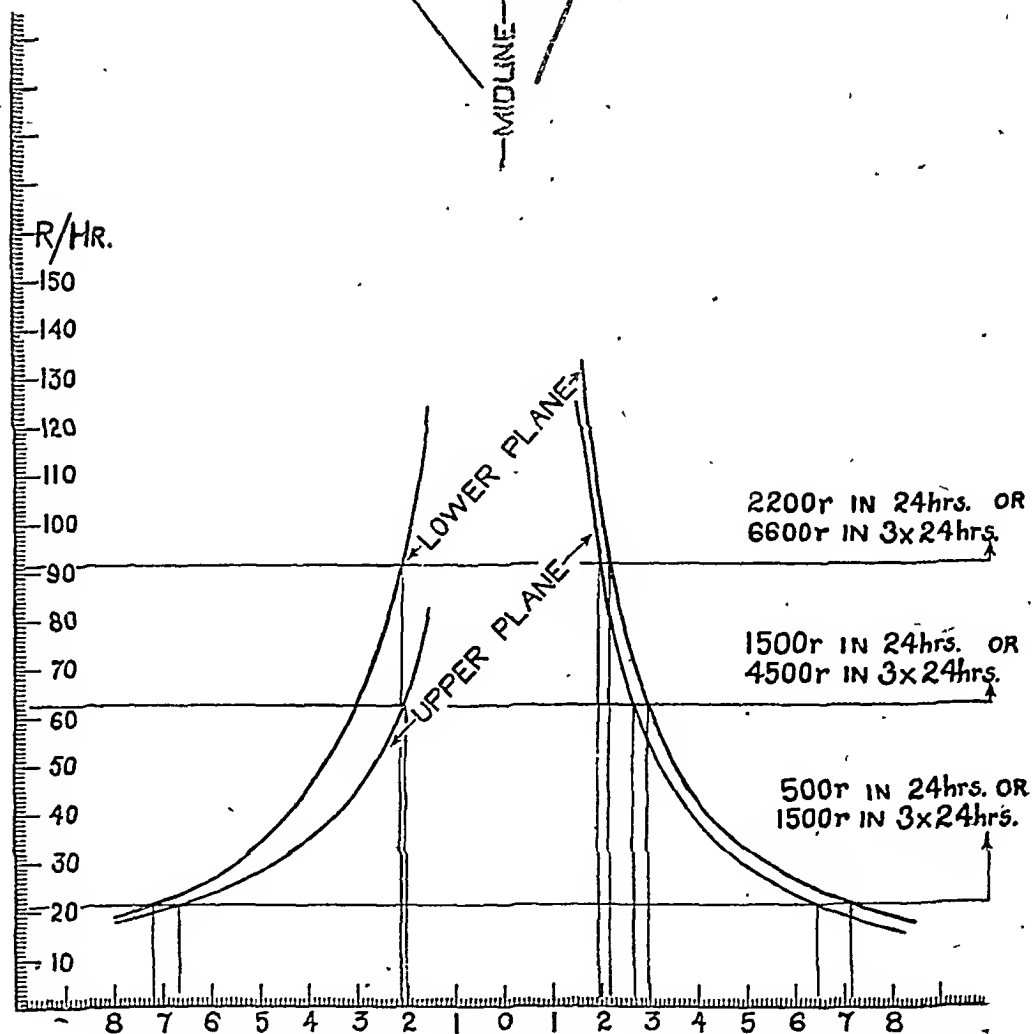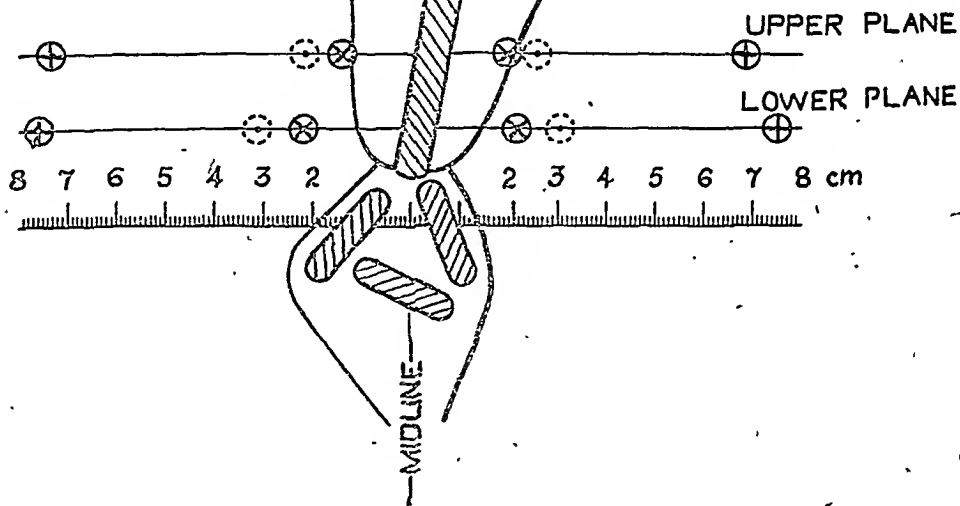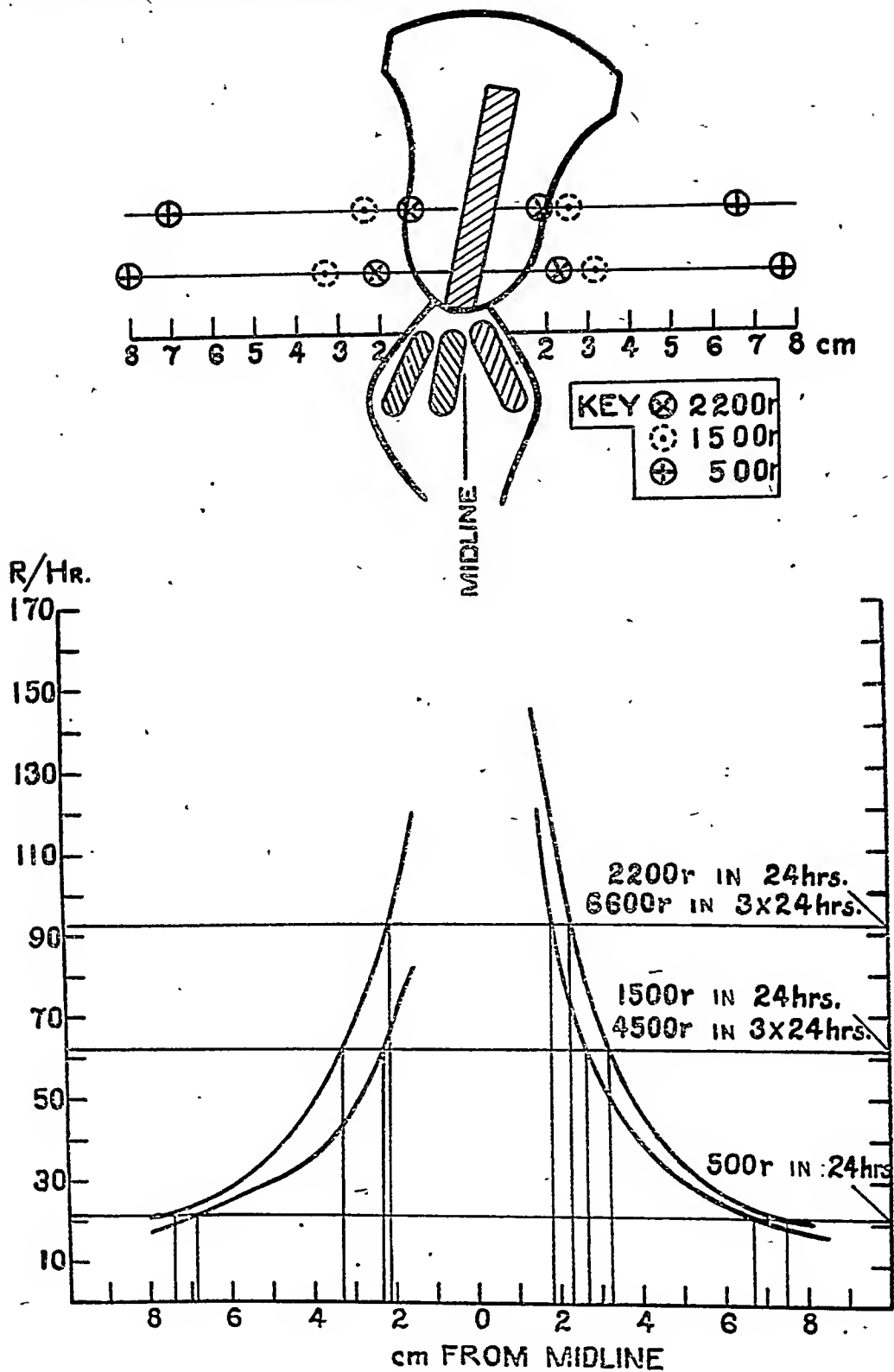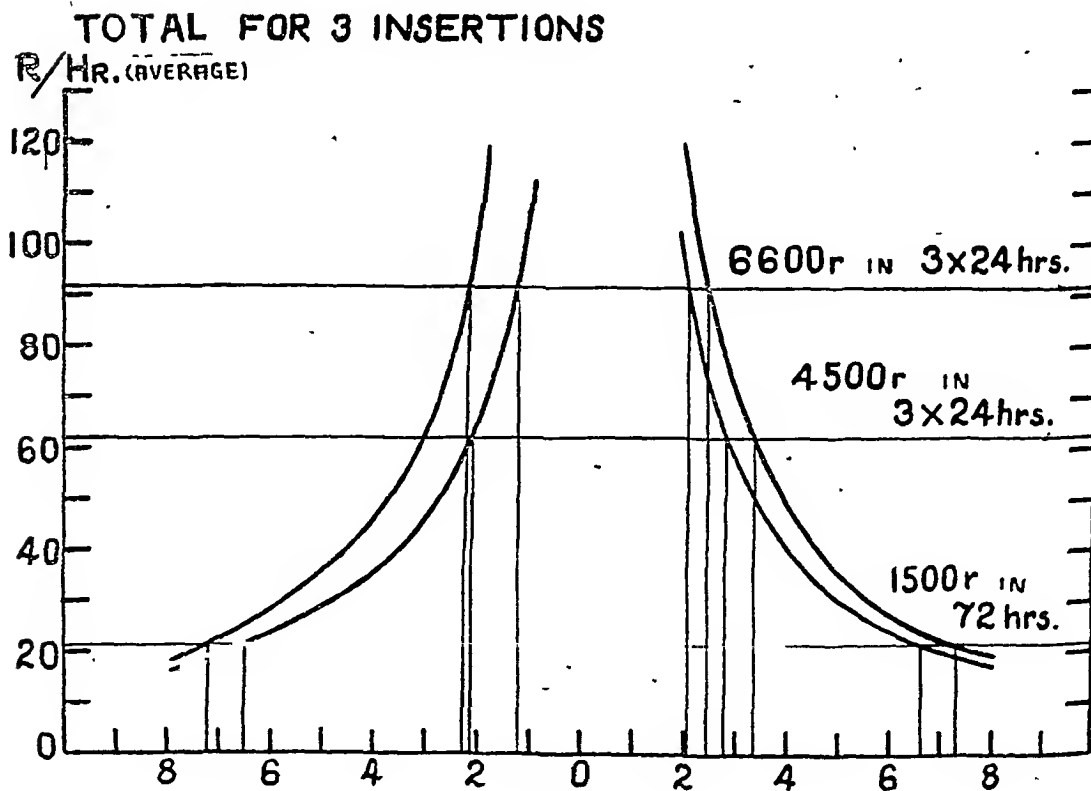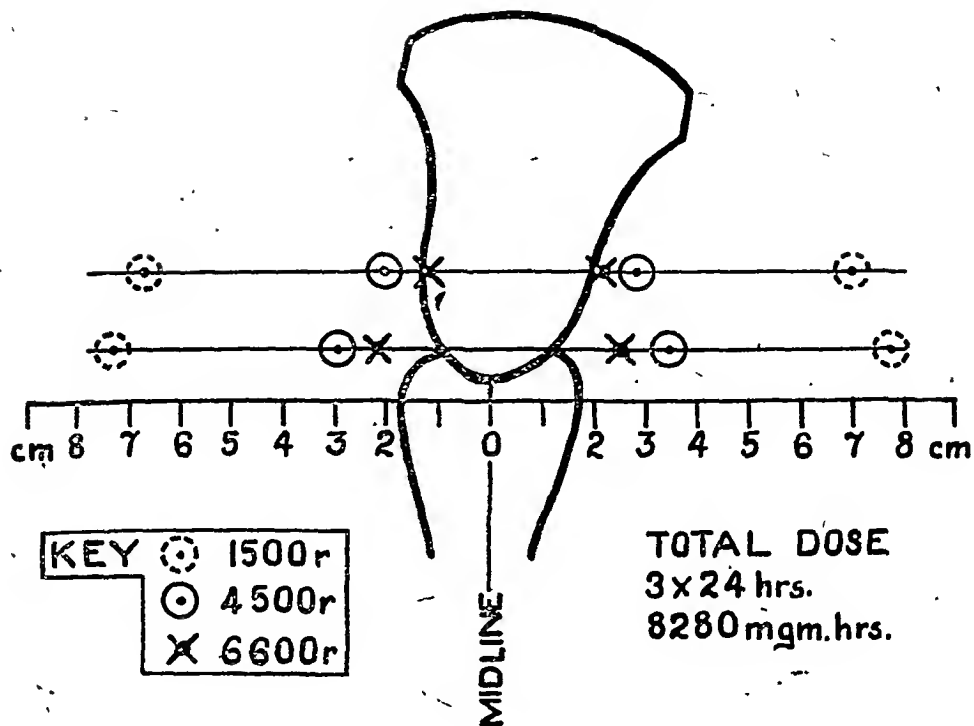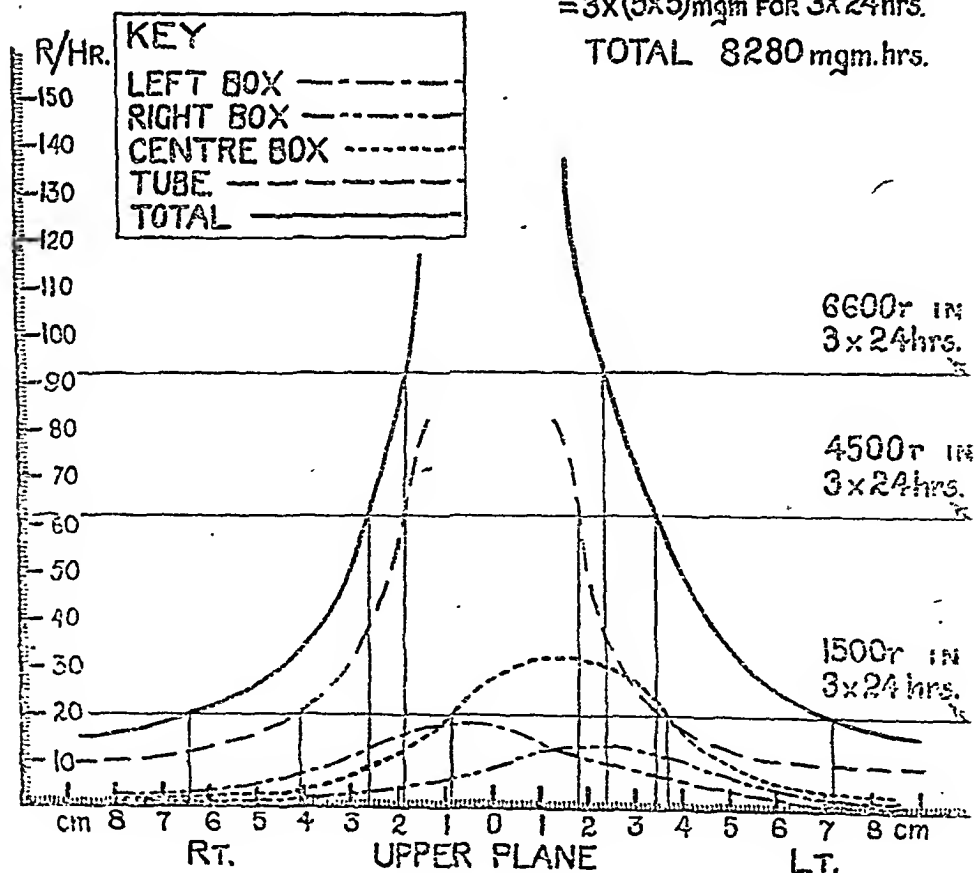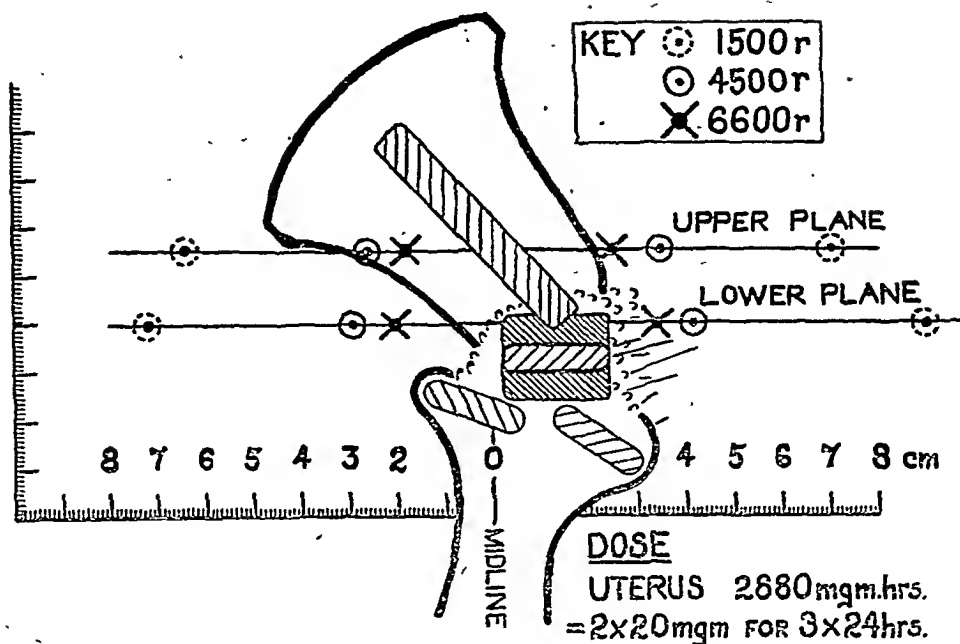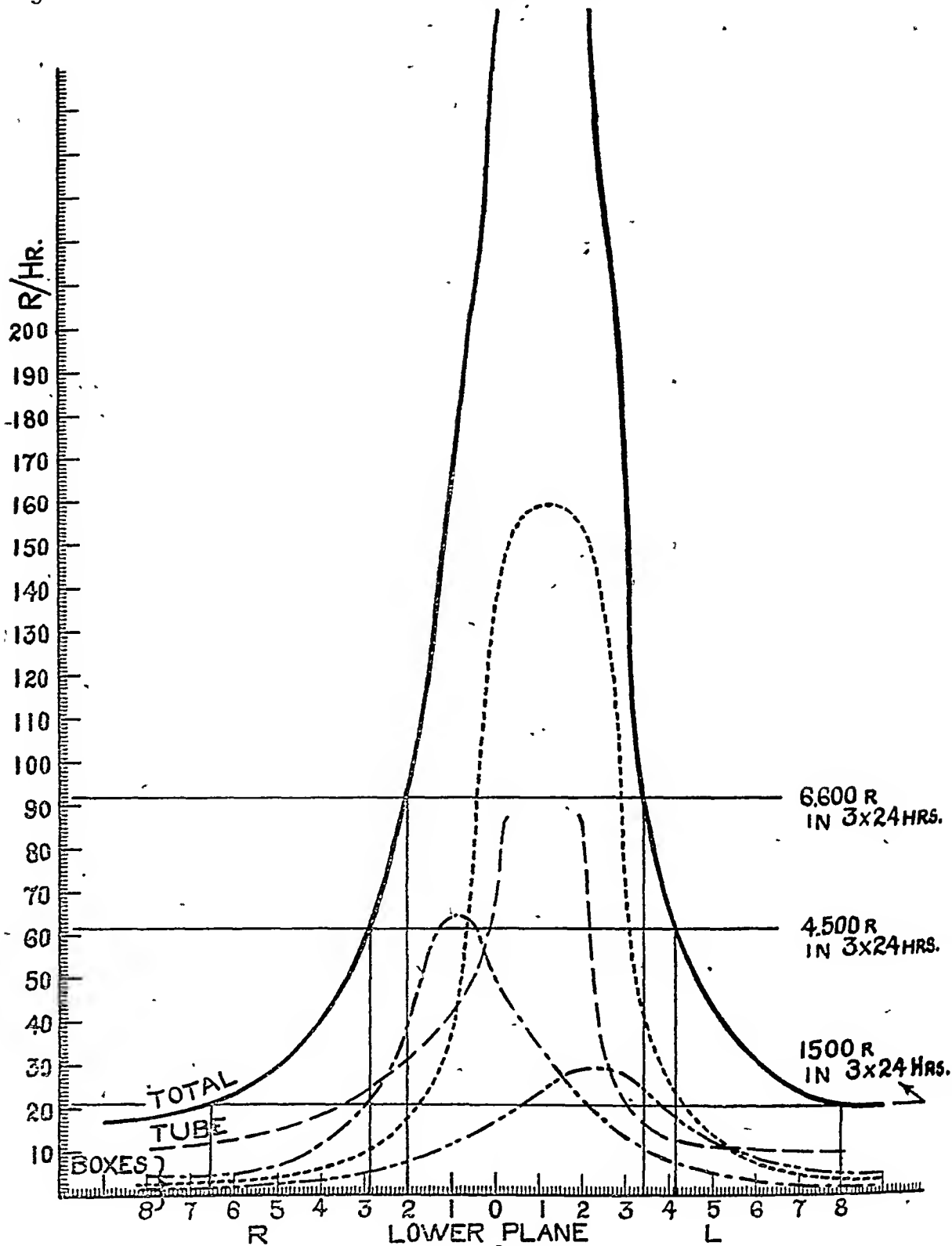
FIG. 13

FIG. 13a.
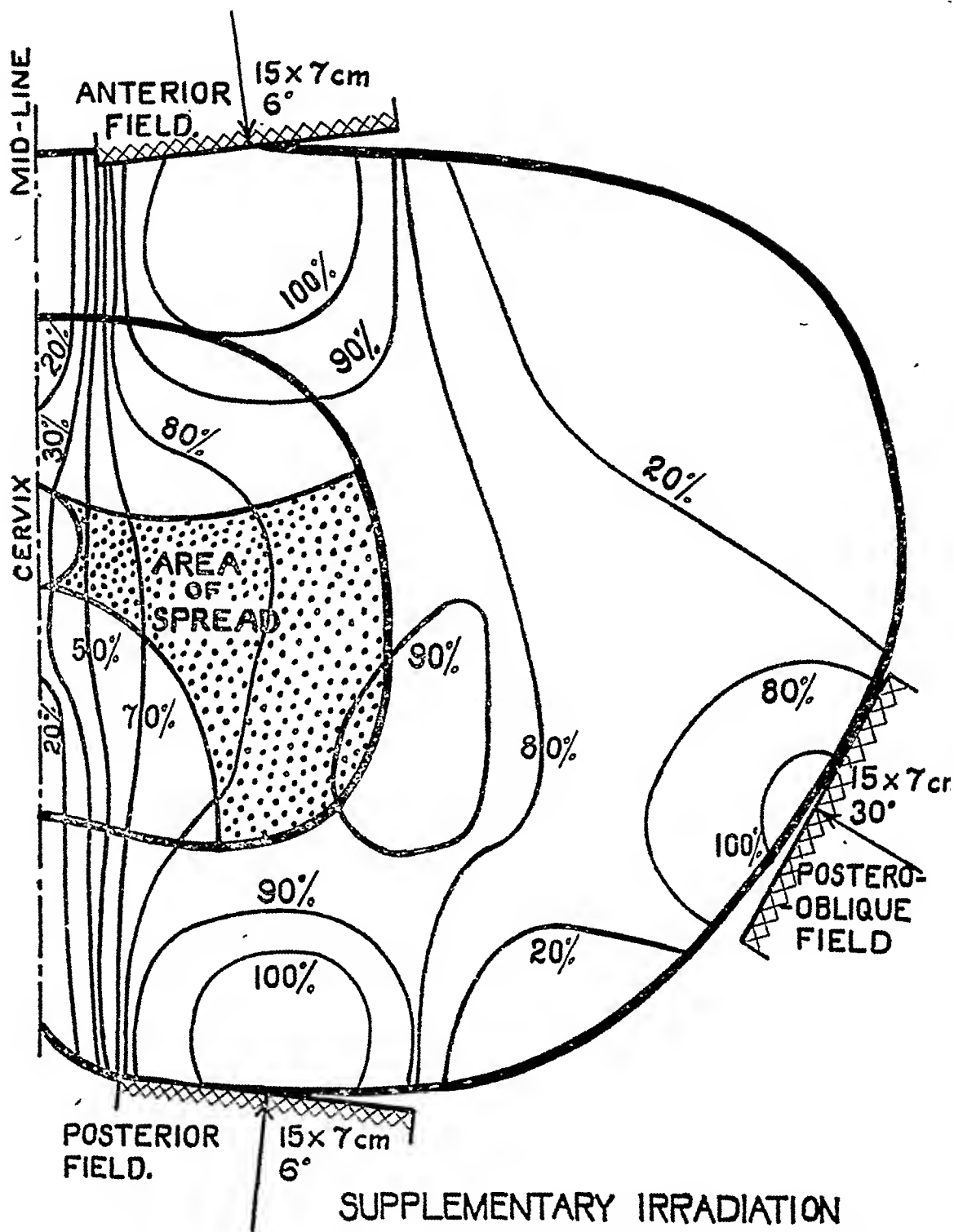
SUPPLEMENTARY IRRADIATION
BY X-RAYS (180 K.V. 1mm.Cu. 50cm.F.S.D.)
AVERAGE CASE

FIG. 18.

B

DISTRIBUTION OF RADIATION IN INTRACAVITARY RADIUM TREATMENT AND SUPPLEMENTARY X-RAY IRRADIATION
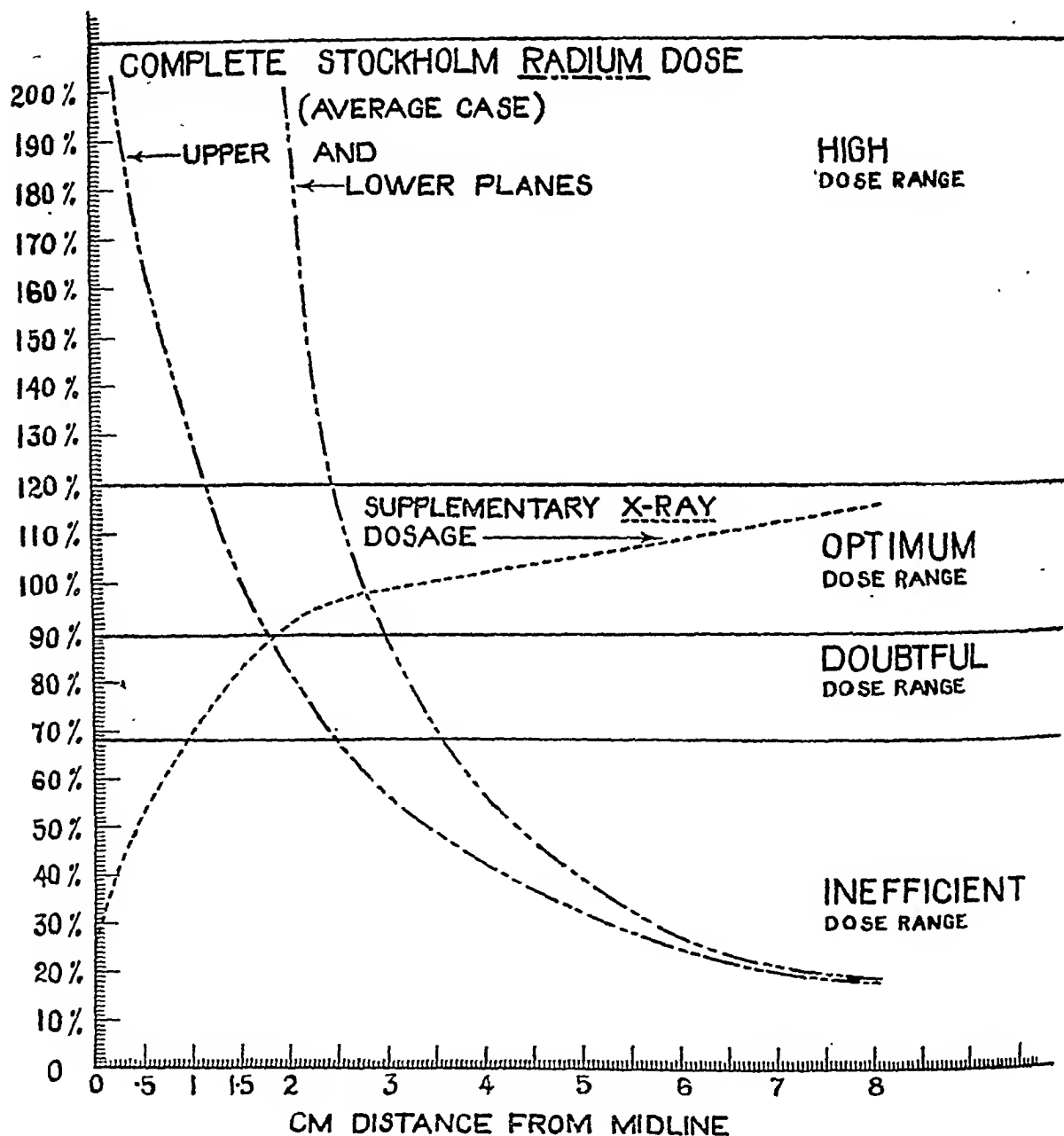
FIG. 19.

Cancer of the Cervix Uteri—The Results of Treatment with Radium

BY

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DURING the 20-year period 1922–41, 837 women with cancer of the uterine cervix were referred to the Cardiff Royal Infirmary, They were grouped into 4 clinical stages as recommended by the Radiological Sub-Committee of the League of Nations. 6 per cent were in Stage 1, 24 per cent in Stage 2, 59 per cent in Stage 3, and 11 per cent in Stage 4. The view was taken that almost all these patients were likely to benefit from irradiation, and only 10 cases were refused treatment.

The cases may be grouped into 1 of 2 periods according to the method of treatment. From 1922 to 1930 only a limited amount of radium was available and this was in the form of needles. There were 2 25 mg. needles, 3 12.5 mg. needles and 6 needles containing 5 mg. of radium element. The screenage employed was 0.5 mm. of platinum, and the usual dose was 80 to 100 mg. for 24 hours, representing a milligram-element-hour dosage of 1,800 to 2,400. The technique has been described by Professor Strachan.[1]

In 1930 a modified Stockholm technique was adopted and has since been used as a routine. In order to make maximal use of the bed-space available, the treatment is compressed into 2 exposures, usually of equal intensity of 30 hours' duration, separated by an interval of 1 week. A tube containing 50 mg. of radium element is placed in the cervical canal, and from 75 to 120 mg. are used in the vault appli-

cators. The equivalent of 1.5 mm. of platinum is used as a filter. Deep X-ray therapy was not available at Cardiff during the period under review.

In spite of every effort to follow-up cases, 9 per cent were lost sight of within 5 years of treatment. These patients, many of whom were progressing favourably when last seen, are regarded for statistical purposes as " dead from cancer ", in addition to those who have died from causes other than cancer during the 5-year period. It is therefore probable that our 5-year figure would have improved with a better follow-up.

Our experiences with the complications of radium therapy in cervical cancer have been reviewed in a previous publication,[2] and this report is concerned primarily with the results of treatment as represented by the 5-year survival rate. The only figure of value for purposes of comparison between different centres or different methods of treatment is the Absolute Survival Rate, based on all cases seen, whether treated or not. Moreover this figure is entirely reliable only when applied to the whole group, irrespective of the stage of the disease. It is acknowledged that there is a considerable personal factor in the clinical staging of cervical cancer, and this is the only method available of eliminating the effects of the upgrading and downgrading of the clinical material.

It is observed that the proportion of early

TABLE I.

Results of Radium Treatment in Cervical Cancer 1922–1941.

	Stage 1	2	3	4	Total
Number of cases seen	53	201	494	89	837
Number of cases treated	53	201	494	79	827
Alive after 5 years	38	67	68	4	177
Absolute 5-year survival rate (percentage)	71.6	33.3	13.7	4.5	21.1
Relative 5-year survival rate (percentage)	71.6	33.3	13.7	5.0	21.4

TABLE II.

242 cases were treated by the Interstitial Method
and 585 cases by the Two-application Stockholm
Technique with the following results.

Interstitial (1922–30)	Stage 1	2	3	4	Total
Number and percentage of cases seen	13 (5.4)	45 (18.6)	174 (71.9)	10 (4.1)	242
Number of cases treated	13	45	174	10	242
Alive after 5 years	11	5	11	0	27
Absolute 5-year figure (percentage) ...	84.6	11	6.3		11.1
Stockholm (1930–41)					
Number and percentage of cases seen	40 (6.7)	156 (26.2)	320 (53.8)	79 (13.3)	595
Number of cases treated	40	156	320	69	585
Alive after 5 years	27	62	57	4	150
Absolute 5-year figure (percentage) ...	67.5	40	17.7	5.0	25.2
Relative 5-year figure (percentage) ...				5.8	25.6

cases (in Stages 1 or 2) increased from a quarter of the total during the first period to a third of the total during the second period. Satisfactory results were obtained with the Interstitial Method only in the first stage of the disease, and the 5-year figures fell rapidly when the cancer had extended beyond the cervix. In general the results have improved substantially since the adoption of the Stockholm technique.

ASSESSMENT OF RESULTS,

Any standard of "cure" for cancer is arbitrary, but the 5-year figure is generally regarded as the most useful. Patients, who after 5 years show no gross or symptomatic evidence of cervical cancer may be regarded as "salvaged" but not "cured".

Bonney[3] states that 10 per cent of all recurrences following hysterectomy appear between the 5th and 10th years, but survival for 10 years without recurrence may be considered a cure. The same assurance cannot be given after treatment by irradiation. In our experience 15 per cent of the women surviving 5 years have died during the next 5-year period, and 6 per cent of those surviving 10 years subsequently died of cancer. A 10-year survival after the irradiation of a cervical cancer is therefore not synonymous with cure.

Three-year figures. It is often desirable to evaluate the results of a particular method of treatment in a shorter time than 5 years, and for this purpose the 3-year

salvage figures serve as a reliable guide. We confirm the observations of Meigs and Jaffe[4] that 15 per cent deducted from the 3-year survival figures for the 4th and 5th years provide a valuable index to the probable 5 year end-results. This is brought out in Table III, which gives the life expectancy of our cases treated by the Stockholm Method. 63 per cent of the patients survived 1 year, 46 per cent survived 2 years and 41 per cent survived 3 years.

1. *The Relation of the Histological Type of the Carcinoma to the Prognosis.*

The relation between cellular structure and response to radium was studied in a previous communication,[5] when a series of 236 cases of cervical cancer, treated by the Interstitial Method, was examined. The response was assessed first by noting the immediate reaction of the growth to irradiation, and secondly by the condition of the patient 3 years later. Our findings were inconclusive, but with the

TABLE III.

Life Expectancy During the 5-year Period Following Treatment by Stockholm Method.

		Stage 1	2	3	4	Total
Number of cases treated		40	156	320	69	585
Survived	1 year (No. and percentage)	35 (87.0)	125 (80.0)	201 (60.0)	21 (30.0)	382 (63.0)
	2 years ,,	35 (87.0)	93 (60.0)	126 (40.0)	16 (23.0)	270 (46.0)
	3 years ,,	33 (82.5)	89 (57.0)	106 (33.0)	13 (18.0)	241 (41.0)
	5 years ,,	27 (67.5)	62 (40.0)	57 (17.7)	8 (5.8)	150 (25.6)
Difference between the 3 and 5-year figures		(15.0)	(17.0)	(15.3)	(12.2)	(15.4)

The patients seen during the 2nd period, 1930–41, and treated by the Two-application Stockholm Method have been chosen for more detailed examination. They provide a sufficient number of histologically confirmed cases, treated by a fairly uniform method to permit reasonably accurate statistical deductions, and the figures of this second period have been broken down to examine the effects of the following variants on the 5-year survival rates:

1. The cellular structure of the growth.
2. The clinical type of the growth.
3. The age and parity of the patient.
4. The length of history.
5. The significance of pain as a symptom when treatment is instituted.

The all-important factor governing the permanence of cure is the clinical stage of the disease when first treated, and an attempt is made to control this influence throughout.

squamous-cell carcinomata our results improved slightly with the degree of anaplasia of the tumour.

We have continued to classify our material on the basis of cell structure into 3 morphological groups—the adult, ripe or spinal cell type, the plexiform mid-ripe or transitional cell type and the unripe, anaplastic spindle cell type. Although mixed tumours are the rule, in the vast majority one type of cell is predominant. In the series under review, microscopic confirmation of the diagnosis was obtained in all but 6 patients, and these had extensive ulceration of undoubted malignancy. In another 18 cases the carcinoma was of the solid type, but the biopsy material was insufficient for reliable microscopic grading. The incidence of the 4 cell types in the present and in the earlier series is shown in Table IV.

Cornification which is usually, but not

invariably, evidence of a mature growth, was noted in 8.6 per cent of the cases.

Before studying the 5-year figures in the does the parity of the patient have any influence on the morbid anatomy of the cancer. In our experience cancer of the

TABLE IV. HISTOLOGICAL TYPES.

Cell type			1922–29	1930–41	Total
Spinal	(number and percentage)		70 (29.6)	137 (24.5)	207 (26.0)
Transitional	,,	,,	126 (53.5)	334 (59.5)	460 (57.7)
Spindle	,,	,,	30 (12.7)	65 (11.6)	95 (12.0)
Adenocarcinoma	,,	,,	10 (4.2)	25 (4.4)	35 (4.3)
			236	561	797

4 histological groups, we propose to examine the influence, if any, of the age and parity of the patient on the cellular type of the carcinoma, and whether the latter is related to the naked-eye appearance of the growth.

We are not in a position to confirm the conception that the ripe types of cancer occur in older women and the unripe types in earlier years. Table V shows the percentage distribution of cellular types of cervical cancer in women under 40 and over 60 years of age.

TABLE V.

Percentage Distribution of the 4 Histological Types in Women.

Cell type	Under 40 years	All ages	Over 60 years
	(150 cases)	(797 cases)	(150 cases)
Spinal	22	26	20
Transitional	68	57.7	58
Spindle	6	12	16
Adenocarcinoma	4	4.3	6

Although spindle-cell cancers and adenocarcinomata were slightly more common in the older women, there does not seem to be any significant relation between the age of the patient and the cell type. Neither

cervix in the nulliparous differs in no respect from the disease in parous women. This applies to its pathology, age distribution and 5-year salvage after radium. Table VI shows the percentage distribution of cell types in 50 women who had never been pregnant.

TABLE VI.

Cell types	Percentage distribution of cell types in	
	50 Nulligravidae	797 Unselected cases
Spinal	28	26
Transitional	54	57.7
Spindle	10	12
Adenocarcinoma	8	4.3

The incidence of cell types corresponds closely to that in the general series, but the incidence of glandular cancers was relatively higher in the nulligravidae.

Relation of cell type to the clinical appearance of the growth. Cancer of the cervix usually appears as an ulcer or as an exophytic growth. In 55 per cent of our patients the lesion was an excavated ulcer, and in 29 per cent it assumed that form of a hypertrophic, papillary or cauliflower growth. The distribution of cell types in the 2 groups is shown in Table VII.

TABLE VII.

The Relation between the Microscopic and Macroscopic Varieties of Cervical Cancer.

Cell type	Total No. of cases	Presented as	
		Hypertrophic growths	Ulcers
Spinal	207	64 (31 per cent)	123 (60 per cent)
Transitional	460	131 (26 ,, ,,)	251 (54 ,, ,,)
Spindle	95	18 (19 ,, ,,)	60 (60 ,, ,,)
Adenocarcinoma ...	35	19 (54 ,, ,,)	7 (20 ,, ,,)
	797	232 (29 ,, ,,)	441 (55 ,, ,,)

Although in general the cell structure of a cervical cancer does not seem to influence its naked-eye appearance, it is noteworthy that more than half the adenocarcinomata appeared as hypertrophic growths, while the spindle-cell cancers were much less commonly seen in this form.

Relation of cell type to the prognosis. The 5-year survival rates in the 5 cell types are shown in Table VIII. The cases are grouped into early (Stages 1 and 2) and late (Stages 3 and 4), so that the effect of the clinical stage of the disease may be controlled as far as possible.

95.7 per cent of the tumours were squamous cell carcinomata, and with these we confirm our earlier impressions,[5] that the final results improves slightly but significantly with the degree of anaplasia of the growth. Our results have not been satisfactory in the small group of adenocarcinomata.

Broders[6] has pointed out that the life history of a cell consists of two processes, reproduction on the one hand, and differentiation and specialization on the other, and in any one cell the activities of these 2 processes seem to be inversely proportional. The more a tumour differentiates, the less is its malignancy, and as applied to cancer of the cervix, this conception is supported by the results of hysterectomy. Broders,[6] Matzloff,[7] Pemberton,[8] Pomeroy and Strauss[9] and others agree that hysterec-

TABLE VIII.

Cell type	Early cases		Advanced cases		All cases	
	Number treated	5-year figure	Number treated	5-year figure	Number treated	5-year figure
Spinal	40	12 (30 per cent)	97	14 (14.4 per cent)	137	26 (19.0 per cent)
Transitional	111	57 (51 ,, ,,)	223	39 (17.4 ,, ,,)	334	96 (28.7 ,, ,,)
Spindle	25	14 (56 ,, ,,)	40	6 (15.0 ,, ,,)	65	20 (30.0 ,, ,,)
Adenocarcinoma	12	2 (16 ,, ,,)	13	1 (8.0 ,, ,,)	25	3 (12.0 ,, ,,)
	188	85 (45 ,, ,,)	373	60 (16.0 ,, ,,)	561	145 (25.8 ,, ,,)
Unclassified epitheliomata	8	4	10	1	18	5
No microscopy	0	0	6	0	6	0
	196	89	389	61	585	150 (25.6 ,, ,,)

TABLE IX.

Results of Radium Treatment.

| Cell type | Early cases (St. 1 and 2) | | Total | |
	Number treated	5-year survivals	Number treated	5-year survivals
Spindle and transitional	136	71 (52 per cent)	299	116 (39 per cent)
Spinal and adenocarcinoma	52	14 (27 ,, ,,)	162	29 (18 ,, ,,)

tomy obtains its best results in the adult types of cervical cancer, and that the outlook after operation is particularly poor in the anaplastic spindle-cell types. With radium, the latter give results certainly as good as those obtained in the less malignant spinal-cell growths, and this is probably accounted for by their greater radiosensitivity. The more malignant anaplastic tumours appear to be more susceptible to irradiation, and the balancing of the 2 factors of malignancy and radiosensitivity seems to be responsible for producing practically the same 5-year salvage figure in the 3 histological groups.

Once treatment by irradiation has been decided upon, histological grading has therefore little practical application, but it may be the determining factor in the decision to employ irradiation rather than surgical treatment even in the earliest cases when the carcinoma proves to belong to the transitional or spindle-cell types.

On the other hand the differentiated spinal-cell tumours and glandular cancers have not responded so well to irradiation and, as shown in Table IX, even when treated at a relatively early stage (1 and 2), have given a combined 5-year figure of only 27 per cent, which may mean that they are better suited to surgical treatment. This tentative deduction must await confirmation or reversal by further investigation.

2. *The Clinical Appearance of the Growth and the Prognosis.*

Clinically the disease is manifest in one of 2 main forms—the ulcerative type in which excavation is the outstanding feature, and the hypertrophic type, which

TABLE X.

Results of Treatment in Ulcerative and Hypertrophic Growths.

| | Number of cases treated | 5-year figure | Early cases | | Advanced cases | | Percentage seen in Stage 1 or 2 |
			Number treated	5-year figure	Number treated	5-year figure	
Hypertrophic							
Fungating mass	63	27 (43.0)*	26	17 (65.0)	37	10 (27.0)	41
Plaque	124	36 (29.0)	48	21 (43.0)	76	15 (20.0)	39
	187	63 (33.7)	74	38 (51.0)	113	25 (22.0)	40
Ulcer	292	54 (18.5)	71	24 (33.0)	221	30 (13.5)	24
Unselected	585	150 (25.6)	196	89 (45.4)	389	61 (15.7)	33

* Figures in parenthesis denote percentages.

may take the form of a plaque or of a cauliflower-like mass which may fill the greater part of the vagina. The infiltrating and sclerosing types form smaller groups, not large enough in our material to permit statistical analysis. As previously observed ulceration was the predominant lesion in 55 per cent of the cases and in 29 per cent the cancer appeared either as a hypertrophic plaque or cauliflower growth. The 5-year results in the 2 groups are shown in Table X.

The group of hypertrophic growths include a relatively large proportion of early cases, and this probably means that as a rule they produce symptoms at an earlier stage of the disease. But irrespective of the degree of advancement of the cancer they have shown much better 5-year results than the ulcerative types, and this applies particularly to the group fungating cauliflower-like cancers.

3. The Relation of the Age of the Patient and the Prognosis.

Sixty-three per cent of the patients were between 40 and 60 years of age—17 per cent were under 40 years of age and 20 per cent were over 60 years. A general impression exists that cancer runs a rapid course in young people and the older the patient the better the outlook. This has not been our experience with cancer of the cervix, as shown in Table XI. Nine women (1.5 per cent) were in their twenties, and 3 of these are among the 5 year survivals. As indicated in a previous section, the incidence of the histologically malignant anaplastic type of cancer was higher in women over 60 years of age.

The proportion of patients seeking treatment at an early stage of the disease is slightly higher in women under 40 years of age, but our results fail to show any significant relation between age and prognosis.

TABLE XI.

Age and Prognosis.

Age group	No. of cases	Percentage in Stages 1 or 2	Alive after 5 years
20 to 39 years	100	39	25 (25.0)*
40 to 59 years	371	32	96 (25.9)
60 to 79 years	114	32	29 (25.4)
Under 50 years	294	35	77 (26.0)
50 years and over	291	32	73 (25.0)

* Figures in parenthesis denote percentages

4. The Length of History and the Prognosis.

From the onset of the first symptoms, which was usually vaginal bleeding in one form or another, there was an average pre-treatment time loss of 7 to 8 months. In general, the longer the history, the more extensive was the carcinoma, but the extent of the disease could not be estimated even approximately from the period during which the patient had symptoms. Approximately one third of our cases were treated within 6 months of the onset of the first symptom, and of these 60 per cent were already in an advanced stage of the disease. Only 1 patient in 10 received treatment within 3 months of the onset of symptoms but, as shown in Table XII, more than 50 per cent of these cases were advanced.

TABLE XII.

Relation of Duration of Symptoms and Extent of Disease.

Duration of symptoms	No. of cases	No. in Stages 1 and 2
Less than 6 months	369	145 (39 per cent)
Less than 3 months	131	56 (43 ,, ,,)
Unselected	1120	(33 ,, ,,)

In cervical cancer, there is no way of telling at what stage of the disease symptoms will appear, and in our experience the length of history does not bear any close

relation to the extent of the lesion and therefore to the prognosis.

5. The Significance of Pain as a Symptom.

In two-thirds of our cases the initial symptom was haemorrhage, but in 14 per cent the first symptom was pain—usually in the back, groins or lower abdomen. As previously noted, the average length of history was 7 to 8 months and, by the time the patients reached hospital, 75 per cent complained of pain. In most instances the presence of pain signifies invasion, but many complained of more pain than would be expected from the stage of clinical advancement of the growth. Half the Stage 1 cases complained of pain and there was usually no associated pelvic lesion to account for it. Pain may be due to secondary infection or to extra-uterine extension of the carcinoma not evident to clinical examination. In any event, the results shown in Table XIII indicate that, irrespective of the stage of the disease, the

2. Morbid Anatomy.

(a) 29 per cent were hypertrophic growths with or without cauliflower-like proliferation. In 55 per cent the most prominent feature was ulceration.

(b) 4.3 per cent were adenocarcinomata and the remainder were squamous-cell cancers. Of these 26 per cent were of the spinal-cell type, 57.7 per cent were of the transitional-cell type, and 12 per cent were anaplastic spindle-cell cancers. Cornification was evident in 8.6 per cent.

(c) There was nothing distinctive in the clinical appearance of the 3 histological types of squamous-cell cancers, but more than half the adenocarcinomata appeared as hypertrophic growths.

(d) No relation could be established between the age or the parity of the patient and the cellular structure of the growth.

(e) Cancer of the cervix in nulliparous women differs in no respect from the disease in parous women.

TABLE XIII.

Stage	Percentage free from pain	Cases without pain		Cases with pain		Total	
		No.	Alive after 5 years	No.	5-year figure	No.	5-year figure
1	50	20	16 (80.0 per cent)	20	11 (55.0 per cent)	40	27 (67.0 per cent)
2	27	39	18 (46.0 per cent)	117	44 (37.0 ,, ,,)	156	62 (40.0 ,, ,,)
3	21	68	17 (25.0 ,, ,,)	252	40 (15.8 ,, ,,)	320	57 (17.7 ,, ,,)
4	22	15	2 (13.0 ,, ,,)	54	2 (3.7 ,, ,,)	69	4 (5.8 ,, ,,)
	25	142	53 (37.0 ,, ,,)	443	97 (21.9 ,, ,,)	585	150 (25.6 ,, ,,)

presence of pain in a case of cervical cancer (when first irradiated) has an adverse influence on the outlook.

SUMMARY AND CONCLUSIONS.

1. The results of radium treatment in a series of 827 cases of cancer of the uterine cervix are presented.

3. Results of Treatment.

(a) Interstitial radium treatment showed a 5-year salvage figure of 11 per cent—it was satisfactory only in cases in which the disease was limited to the cervix. With the Two-application Stockholm Technique, the absolute 5-year survival rate was 25.2 per cent.

(b) 15 per cent of the women surviving

5 years have died of cancer during the succeeding 5-year period, and even 10-year survival after radiotherapy is not synonymous with cure.

(c) The best results were obtained in the hypertrophic growths. They produce symptoms earlier than do growths of an infiltrating nature, but they have a more favourable prognosis irrespective of the clinical stage of the disease.

(d) The prognosis in adenocarcinoma of the cervix is not so favourable as that in squamous-cell cancers, in spite of their tendency to develop as hypertrophic or cauliflower growths. The best results were obtained in the more anaplastic squamous-cell cancers—the mid-ripe transitional-cell types and the unripe spindle-cell types.

(e) The duration of symptoms was a poor index to the extent of the disease and therefore to the prognosis.

(f) The presence of pain does not invariably indicate advanced disease, but at all stages it has an adverse influence on the prognosis.

(g) This survey again demonstrates the importance of early diagnosis. By far the most important factor controlling the permanence of cure is the extent of the carcinoma when treatment is instituted.

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A Note on Fothergill's Colporrhaphy*

BY

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WHEN this article was first conceived, its intention was the praise of a famous surgeon, Fothergill, who died 20 years ago, during the Autumn of 1926. Some may think it has changed its character during the period of gestation and that, in fact, twin objects have been born; the first a review of the vaginal plastic operations for the cure of genital prolapse during some 80 years; and secondly an effort to counteract an attempt that has been made since Fothergill's death to belittle the value of his work.

In order to avoid any misunderstanding of these remarks, the opinions expressed by 4 former presidents of this society may be quoted. In 1930 a reference to the "Fothergill" operation is summed up—"These modifications were modifications of technique only, but the principle was the same as in Donald's operation." In the proceedings of this society will be found 2 further comments; in 1931 the remark "Fothergill modification of the Donald colporrhaphy." And in 1945 "Donald is really the originator of the Fothergill—or as I prefer to call it, Manchester operation." In our Journal in 1935 there is a reference to the "technique initiated by Professor Donald last century and subsequently modified by the late Dr Fothergill." These 4 statements appear to have been made without full knowledge of the history of this operation, and therefore a short review of its roots and growth is most necessary.

The first vaginal plastic operation for the cure of genital prolapse was performed in London in 1831. The description which follows is taken from the translation of a French treatise on Gynaecology by Madame Boivin and Monsieur Duges, a midwife and a professor; French politeness giving precedence to a *sage femme* before a university professor.

The French authors state in their text that "Dr Marshall Hall has lately cured a case of complete prolapsus by artificial contraction of the vagina." The English translator was also the surgeon of the case, and he describes his operation in a footnote which occurs only in the English translation, as follows: "It occurred to me that if the canal of the vagina could be considerably, permanently and firmly reduced in diameter, the uterus would be supported in its place, and prevented from resuming its prolapsed situation; and that this might be done by removing a portion of its mucous membrane along the anterior part, and by bringing and returning the denuded surfaces in contact by successive deep sutures, until they should unite by cicatrix.

"This operation was performed by Mr. Heming, of Kentish Town. The uterus being protruded as much as possible, by the efforts of the patient, two parallel incisions were made through the mucous membrane, from the sides of the os uteri, along the course of the protruded vagina, to the os externum, the portion of this membrane situated between these incisions was then removed, leaving a space of an inch

* Read before the North of England Obstetrical and Gynaecological Society, October 4th, 1946.

and a half in breadth, and of the entire length of the vagina, completely denuded. A suture was then inserted near the os uteri. This suture being tightened, the os uteri was obviously pushed upwards. A second, a third and other ligatures, were then inserted, in the same manner, at short intervals, to the os externum; each ligature, on being tightened, moving and supporting the os uteri upwards.

"This operation was attended with little pain; the only sensitive parts of the membrane being those near the os uteri and os externum."

This article seems to have attracted so little attention that it was completely ignored. I can find no reference in the literature to it for a period of 30 years. You will have noticed the accurate description of the behaviour of the cervix as the stitches are tied in the anterior vaginal fornix in a properly performed Fothergill operation. The second point that one might mention is the use of the terms "mucous membrane" for the epithelium of the vagina, an error which frequently occurs even to-day. The third comment I would make is that the fact that the operation was attended with little pain causes offence to the self-satisfaction of the local anaesthetist. The fourth comment of importance is that the aim of the surgeon is to narrow the vagina. This remains the object of the vaginal operation, with few exceptions, for 70 years. Finally it will please those who like to call the modern operation by the name "Manchester" to learn that Mr. Heming writes from Manchester Square, London, the only reason I know why the ugly name should be associated with this operation.

More than 10 years later, in the eighteen-forties, Huguier of Paris demonstrated supravaginal elongation of the cervix, and stated that hypertrophy of the cervix occurred in every case of uterine prolapse,

an error that is frequently repeated even to the present day.

Huguier performed amputation of the cervix in every case and claimed considerable success.

In the fifties Baker Brown of London decided that the cure of genital prolapse could be achieved by the narrowing of the vagina to such an extent that the passage was too narrow to allow anything to descend. He contracted the vulval outlet by a very extensive perineal operation. Whether his satisfaction was equalled by that of his patients or their husbands we have no direct evidence.

Another decade passes, and in 1866 we find Marion Sims in London. He had voluntarily left America in 1862 on account of the political troubles; he served as a surgeon in Paris in 1871, and did not return home until after the Franco-Prussian War had ended. In 1866 he published, in London, a book with the title *Clinical Notes on Uterine Surgery with Special Reference to the Management of the Sterile Condition*. There were 8 sections, each with a title relative to conception. Section 5, which is the one to which I shall refer, is headed "The uterus should be in a normal position, i.e., neither anteverted nor retroverted to any great degree." The sixth subheading to this section is "Procidentia Uteri."

Sims points out that many surgeons practised amputation of the cervix, or contraction of the vulvar outlet by perineal operation for the relief of genital prolapse. He was unaware of Heming's work 25 years earlier, until his own operation on the anterior vaginal wall was standardized. Sims was the first to do many plastic vaginal operations for the relief of prolapse, but his object was quite definitely to narrow the vagina, but much higher up than could be done by perineal operations.

In 1856 he had been consulted by a lady

with a large prolapse. He remarks rather naively: "This was the first time I had had a good opportunity of observing and studying the manner in which the procidentia occurred." It was evidently a case of classical prolapse with the bladder leading the descent. He noticed the large cystocele, and, remembering the very great success he had had in the repair of vesicovaginal fistula, he seriously proposed to this lady to make a complete vesicovaginal fistula by removing at once a large portion of the base of the bladder with the anterior vaginal wall. She agreed, and he laid the plan of operation before the consulting board of the hospital. I quote his account of the operation: "Proposing to excise the anterior wall of the vagina I hooked it up with a tenaculum, pulled it well towards the posterior wall, and then grasped the base of the mass thus elevated with a pair of curved forceps made for the purpose, which held the parts firmly embraced, while with scissors cutting under the forceps I removed at once a very large portion of the anterior vaginal wall. The chasm made was fearful. My surprise was equalled only by my delight when I found that I had not succeeded in doing what I intended; for instead of excising the base of the bladder I had simply raised the vaginal tissue up between the blades of the forceps, luckily separating it from the lining membrane of the bladder which remained intact." I wonder if any other surgeon has been surprised and delighted at failing to accomplish that which he attempted to do!

He continued to operate on similar cases, but used no more the special forceps with which he clamped the cystocele. Instead he simply removed the vaginal epithelium.

However, he found the necessary scarification both tedious and bloody; and also there was a danger of local inflammation. One of his failures led him to devise another method of operation. He "simply re-

removed the mucous membrane in the form of a V, the apex being near the neck of the bladder, the two arms extending up on the sides of the cervix. These two denuded surfaces were brought together by silver sutures thus making a longitudinal fold narrowing the vagina and crowding the cervix backwards."

Again you will notice that the surgeon remarked on the cervix being pushed backwards when the stitches are tied. The anatomical importance of this is not grasped, but the narrowing of the vagina is still stressed.

Another failure led him to alter the shape of the denuded area from a simple V to a trowel shape. He sums up the situation by saying: "So far as mere surgical resources are concerned, we have now three processes from which to choose; always, of course, adapting this choice to the particular exigencies of the case.

"1. Amputation of the cervix when its infravaginal portion is too long.

"2. The perineal operation.

"3. The operation of narrowing the vagina by denudation of its anterior wall as herein illustrated. Sometimes, as in cases of rectocele, it is necessary to narrow the posterior wall of the vagina as well as the anterior."

It is doubtful whether he amputated the cervix in addition to narrowing the vagina; although he was well aware of the very considerable hypertrophy or elongation of the cervix, he only advised operation when its infra-vaginal portion was too long.

Emmet remained in America and continued to operate, using the same technique that Sims introduced. Reading between the lines one gathers that healing was by no means perfect. Emmet reports such a case he had in 1869 in which the colporrhaphy only healed near the cervix, but in spite of this the result was good. Again you will notice a hint that the cure of prolapse of

the uterus can be brought about by operation in front of the cervix. Even Emmet, although he reported the case, did not realize its full significance.

In the seventies, Hegar introduced his operation of posterior colpoperineorrhaphy. His name remained attached to this operation for many years. In fact the first vaginal plastic operation reported to this society some 20 years later was described by Gemmell, and he used Hegar's name. This was a very wide operation with its apex as close as possible to the cervix uteri. Hegar published in 1889 his Cyclopaedia, and one gathers that the cure of a procidentia required a 2-stage operation; the first an amputation of the cervix and an elytrorrhaphy, both anterior and posterior. This word means the same as colporrhaphy. But he says that the main operation — colpoperineorrhaphy — is performed after the parts have healed. It is possible that the translation of his book is not particularly good, but it is difficult to understand why 2 operations were required on the posterior vaginal wall. It was a Frenchman who compared translations to ladies: *Lorsque elles sont belles, elles ne sont pas fidèles.*

For many years after Hegar's description of his work was first published there appeared a large number of articles describing alterations in the shape, size, and position of the vaginal incisions in the plastic operations, interposition operations and finally abdominal operations. None of the authors appeared to appreciate the anatomical basis for the proper cure of uterine prolapse until the early years of the present century. I am, therefore, ignoring these as they had no influence on Fothergill's later work.

Some of the work is interesting and amusing, and I will draw your attention to a paper by Emmet on ruptured perineum. The prolapse of the posterior vaginal wall, which is so frequently associated with this condition or with a badly stitched perineal tear, he claimed could be cured by a colporrhaphy with a transverse incision across the posterior vaginal wall. The pathological anatomy of this condition, which was a separation of the vaginal wall from the underlying fascia, was best understood, he thought, if one imagined that one's pantaloons had become separated from their suspenders.

His simile was not approved by all his audience. Dr. T. A. Reamy told the meeting: "He has stated that the separation from this fascia is just the same as though his pantaloons should be separated from his suspenders. I will carry the illustration a little further, and say that if he restores the suspenders it is all very well; but if the pantaloons are split open the full length of the seat, it will not include the whole condition unless he restores them also; and so if he lifts up the split perineum without closing the laceration, it is just the same as to lift up the seat of his pantaloons without uniting the rent."

As an example of the ingenuity of surgeons may be mentioned the case operated on by Freund in 1908. The woman had procidentia and a large inguinal hernia. The operation was a hysteropexy of the uterus in the inguinal canal thus fulfilling two functions:

(1) The corking up of the canal so that the hernia could not descend, and

(2) The fixation of the fundus so that the cervix could not prolapse.

It is often said that Manchester was teaching the world from about the year 1888 how to cure prolapse. I have searched through the literature, including the transactions of this society, for evidence of this fact without success. In 1893 Alexander read a paper on his operation on the round ligaments. About 50 per cent were cases of uterine prolapse. Donald advised col-

poperineorrhaphy for procidentia. The term colpoperineorrhaphy at this date was generally used to mean Hegar's operation on the posterior vaginal wall.

In 1894 Gemmell described a case of complete prolapse with cystocele and rectocele treated by Hegar's posterior colpoperineorrhaphy. Donald said he had been interested for some years in vaginal operations for prolapse. The reason for failure was that the methods adopted were not sufficiently thorough. In all cases the operation should consist of 3 stages at least: (1) Anterior colporrhaphy. (2) Posterior colporrhaphy. (3) Perineorrhaphy. In cases where there was much enlargement of the uterus supra-vaginal amputation of the cervix was also necessary.

The only other comment came from Wallace: "To talk about curing a cystocele after colpoperineorrhaphy was like placing the cart before the horse—it could not be done."

In 1896 Curtis Webb read a paper on vaginal fixations of the uterus. There was no comment from Manchester.

In the early days of the century the anatomists were beginning to be interested in the anatomy of the female pelvis. Various surgeons attempted to secure the transverse ligaments (or Mackenrodt's ligaments) and sew them in front of the cervix.

In 1902 Reynold in America suggested a crescentic flap in front of the cervix. And in the following year Alexandroff proposed a curved transverse incision across the anterior vaginal fornix.

In 1905 Tweedy suggested an operation opening the anterior vaginal fornix into the peritoneal cavity, detaching Mackenrodt's ligaments from their lateral attachments and sewing them on to the anterior surface of the cervix.

In 1907 Fothergill read a paper before the Royal Society of Medicine on the anatomy of the female pelvis and before the Edinburgh Obstetric Society at about the same time described his first anterior colporrhaphy. This operation was not the one which we know these days by his name. Where necessary the first stage of the operation was an amputation of the cervix by one of the well-known methods. The second stage of the operation was an anterior colporrhaphy with the area of epithelium to be removed triangular in shape, the base of the triangle being a transverse incision across the anterior vaginal fornix, and reaching widely outwards towards the lateral fornices so that the transverse ligaments of the cervix could be reached and brought together in front of the cervix when the repair operation began. Fothergill at this time stated that he frequently opened the abdomen and did a ventrofixation of the uterine body.

In 1908, shortly after Fothergill's articles had been published, Donald wrote up an article on the cure of uterine prolapse. Where necessary he amputated the cervix by the removal of wedges from the anterior and posterior lips. His anterior colporrhaphy you will notice is also triangular in shape, with the base close to the urethral orifice, and the apex in the region of the cervix. No deep sutures are used, and at the end of this stage of the operation there is nothing to prevent the cervix from being pulled right outside the vulva. The posterior colporrhaphy is identical with that of Hegar, even to the extreme narrowness of the vagina which results from this part of the operation. Again no deep sutures were used. Donald's own description of this is that the lateral incisions end midway between the fourchette and the vestibule. This can only mean that the anterior-posterior diameter of the vagina at its entrance is reduced to half the size it was before the first pregnancy occurred. In fact in my resident days

this operation was referred to as the slate pencil colporrhaphy, and there was nothing original in it for it is almost identical with Hegar's operation, and is based on the theory begun in 1831 and carried on for over 75 years that in vaginal plastic work the cure of prolapse depended on narrowing the vagina.

I have been unable to find any record of one variation of this technique which Fothergill liked much and used when the case was suitable. When the cervix was not hypertrophied or elongated the incisions beginning as usual in the neighbourhood of the urethra passed upwards and outwards into the vaginal lateral fornices as
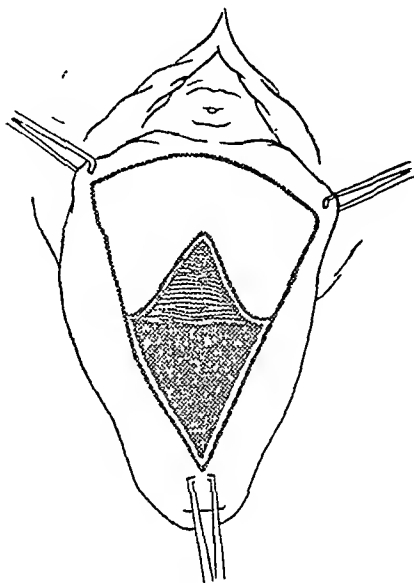
FIG. 1.
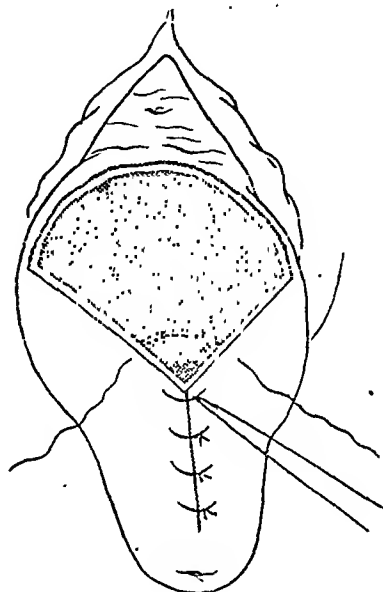
FIG. 2.

Two of the diagrams published in Donald's first article in 1908. Fig. 1 illustrates that the incisions in the cervix are between 1 and 2 inches distant from the ligaments of Mackenrodt. Fig. 2 shows that when all suturing of the cervix is completed, there is no change in the position of this prolapsed organ.

It was not until 1913 that Fothergill published the details of his final operation as it is known to-day. He himself described his operation as an amputation of the cervix with wide anterior racquet incision. The object of these wide incisions was, as we all know, so that the ligaments, by whatever name you like to call them, the transverse ligaments of the cervix, Mackenrodt's ligaments, the cardinal ligaments of the cervix, Patenson's, and so on, which lie above the lateral vaginal fornices might be brought in front of the cervix as the wound was being repaired.

usual, but the transverse incisions which joined the two together did not pass behind the cervix, but came directly in to the cervix at three o'clock and nine o'clock, so that only the anterior lip of the cervix was amputated, and very little of that was removed. As I have said, the cervix was not enlarged and did not need amputating, but by this method he obtained access to the ligaments he wanted above the lateral vaginal fornices.

In 1921 at the British Congress of Obstetrics and Gynaecology Donald read a paper on " A short history of the opera-

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tion of colporrhaphy with remarks on the technique.''

His final remarks on technique are: '' One cannot have a very extensive operation on both walls (of the vagina). When cystocele is not the main feature, I regard the building up of a firm posterior wall as the important point. One must recognize, if one is to have any success, that the deep tissues, the triangular ligament or the levator ani muscles must be brought together by deep sutures.''

There have been several short histories of the operations which are included under the term vaginal plastic operations for prolapse in the *Journal of Obstetrics and Gynaecology of the British Empire,* and in every one of these is found repeated the same strange mistakes.

Taking them in chronological order: In 1921 an article by Donald with the title: '' A short history of the operation of colporrhaphy.'' The history of the operation before he himself began to practice it in 1888 is condensed into one sentence as follows: * '' It is true that one had read accounts of operations done in America and Germany '' and he ends the paragraph with the discouraging remarks taken from the textbook of Hart and Barbour.

In August 1936 is published a paper by Gray Ward which he had read before the British Congress in Belfast the same year. He lays down certain principles for the cure of the various varieties of genital prolapse, and attempts to decide which surgeon should receive credit for being the first to appreciate and employ a definite principle. For example he claims that Sims was the first '' to completely expose the base of the bladder '' as is done to-day. You will note how dexterously he splits the infinitive in referring to Sims's attempt to clamp the prolapsed anterior vaginal wall together with the bladder and to cut them both off together. It is incor-

rect to say that this is how the operation is done to-day; and it is also incorrect to say that Sims appreciated the principle attached to exposing the base of the bladder, for he never attempted to do this again.

Later in the same article, referring to procidentia, he says: '' The principle of reefing the overstretched cardinal ligaments by approximating them in front of the cervix or its stump, if amputated, is a *sine qua non* for the cure of its prolapse, if that organ is to be conserved. To Donald would seem to belong the credit for first appreciating and employing this principle *in a definite manner in 1888. He combined* an extensive anterior and posterior colporrhaphy with amputation of the cervix, using deeply buried sutures which approximated the fascial structures in front of the cervix, and below the vaginal mucosa.

He had evidently never read Donald's paper of 1908 or seen the only diagrams he published, or he would have realized two facts: (1) That the incisions used in this particular operation prevented access to the cardinal ligaments. (2) He did not use buried sutures until some time after Fothergill had been writing much on genital prolapse.

In August 1940 Stallworthy published an article on the result of operation on genital prolapse. He begins with a historical survey, and after mentioning some of the earlier work, he calls attention to the fact that the credit of combining anterior and posterior colporrhaphy goes to Tracy in Australia in the year 1862. From this date only one advance in surgery is mentioned: '' The next great advance was made in Manchester when, in 1888, Donald combined a double colporrhaphy with amputation of the cervix. By removing a diamond-shaped area from the anterior vaginal wall and vault he displayed the

paracervical condensations of fascia with which he strengthened the repair.''

How strange and almost incredible is the transference of the credit for the discovery of certain surgical principles from one surgeon to another. The only explanation is that the author has not read the articles of either surgeon.

If I were asked the difference between the operation that Donald performed for the cure of genital prolapse and Fothergill's operation I should say that Fothergill's was an entirely new and original procedure, with a firm base on a knowledge of anatomy and the correct conception of the character and position of the structures which maintained the normal uterus in position; and finally an appreciation of the damage done to these structures during parturition, and the best method of repairing this damage.

The operation which Donald performed was not original, being identical with that of Hegar. Its technique was not based on any knowledge of anatomy, but on the 60-year-old theory that narrowing of the vagina was the only hope of the patient. Donald went so far as to compare his operation to the radical cure of a hernia.

I never regarded Fothergill as a great abdominal surgeon, or as a particularly outstanding diagnostician; but he was a first-rate pathologist. His claim to greatness rests on his vaginal plastic work, and it is impossible to stand quietly aside while attempts continue to be made to detract from his reputation. Finally I will quote a house surgeon's opinion of him taken from a Christmas play written in the Gilbert style:

A '' Webster's-Sling '' young man,
A tongue-with-a-sting, young man,
A man who glories in dubious stories,
Colporrhaphy-King young man!

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The Interpretation of Tests for Renal Function[*]

BY

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THIS paper deals with the *rationale* of the test of renal function that is employed at the Jessop Hospital for Women in cases of toxaemia of pregnancy, and with the picture that the various clinical stages of the disease present in renal function tests.

From the point of view of function, the kidneys may be described as two localized masses of nephron units, and because of their multiplicity and their relative independence, one would expect that the kidneys as a whole would show considerable powers of compensation and reserve, which indeed they do.

One would also expect that renal function tests, assessing as they do mass function and not individual nephron activity, might easily indicate good function, even when considerable anatomical damage to the kidneys had actually occurred. This again is generally accepted. It therefore follows that if the tests do show even minor degrees of renal insufficiency, then the results theoretically ought always to be of clinical significance. That unfortunately is not the case, and renal function tests have to some extent fallen into disrepute.

It seemed to me, therefore, that it would be worth while combining a series of these tests and, by checking one aspect of kidney function against others, obtain a clearer picture of the capabilities of the kidneys at the time of test than was possible previously.

The test we now employ is a combination of the urea concentration test, the Van Slyke and the Fowweather tests with two non-protein-nitrogen estimations included for completeness. The procedure is as follows:

1. No food or fluids after midnight.

2. At "zero hour" (usually 4.30 a.m.) the bladder is emptied by catheter.

3. One hour later. Bladder again emptied by catheter; 10 ml. blood taken. 15 g. urea in 300 ml. water by mouth.

4. One hour later. Bladder again catheterized. Second blood specimen taken.

5. One hour later. Bladder emptied by catheter.

6. One hour later. Bladder emptied by catheter.

For the purposes of the clearance-calculations it is important that the exact time to the minute of collection of specimens is noted.

FIG. 1.

KIDNEY FUNCTION TEST.

Specimen of Normal Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
Zero	400	1016	2.00	8.000	Nil
1 hour	40	1016	1.80	0.720	Nil
2 hours	120	1010	1.70	2.040	Nil
3 hours	100	1016	2.50	2.500	Nil
4 hours	80	1018	2.80	2.240	Nil

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 300 ml.

Weight of urea excreted in 3 hours after urea, 6.780 g. (over 6.0 g.)

Average urea concentration, 2.26 per cent (over 2.0 per cent).

Blood Specimens.

Blood urea before urea, 18 mg. per 100 ml.

Non-protein-nitrogen before urea, 18 mg. per 100 ml.

Blood urea after urea, 35 mg. per 100 ml.

Non-protein-nitrogen after urea, 30 mg. per 100 ml. (less than 40).

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 40 ml. (Time, 60 minutes).

Volume of urine per minute, 0.67 ml.

Urinary urea, 1,800 mg. per 100 ml.

Blood urea, 18 mg. per 100 ml.

Standard clearance per minute, $1,800/18 \times \sqrt{0.67}$ ml.

$= 82$ ml.　　　　(54 ml. Standard).

$= 152$ per cent of normal (75 ml. maximal).

Urea Clearance after Urea (Fowweather).

Volume of urine, 100 ml. (Time 60 minutes).

Volume of urine per minute, 1.67 ml.

Urinary urea, 2,500 mg. per 100 ml.

Blood urea, 35 mg. per 100 ml.

Clearance per minute, $2,500/35 \times \sqrt{1.67}$ ml.

$= 92$ ml.,

$= 103$ per cent of normal (75 ml.).

Fig. 1 shows a typically normal result and I would draw your attention to certain points.

1. Volumes: Post-urea diuresis.

2. Specific gravity: Post-urea dilution and rapid recovery.

3. Absence of albumin: Essential for normality, but its absence does not necessarily mean that the kidney is normal. This statement is in contradiction of the usual view, and will be substantiated later.

4. Urea-concentration test: (a) Volume of urine, 200 to 300 ml. Volumes below this are often associated with toxaemia; vol-umes above, with hypertension or chronic nephritis.

(b) Total urea: Should be over 6 g.

(c) Average concentration: Over 2 per cent (2 per cent without a total over 6 g. I do not consider normal but as merely indicating that the kidney can still concen-trate).

5. Blood specimens: Estimations of urea and non-protein-nitrogen are done on both blood specimens. High values before urea (non-protein-nitrogen over 40) are significant of severe kidney disfunction.

(a) Normal values have not the opposite significance. Even in severe toxaemias and particularly when they are on a low-protein diet one usually gets normal values.

(b) High values after urea are indicative of nitrogen-retention: for non-protein-nitrogen values forty is usually taken as the upper limit of normality.

Low values usually indicate absence of nitrogen-retention, but there are two con-ditions to be remembered when this does not hold good:

(a) In the presence of excessive oedema nitrogen-retention can occur without a sig-nificant rise in second-blood values.

(b) The patient may have vomited the urea given by mouth.

6. *The Clearance Test.*

The first of these (Van Slyke's) is calcu-lated from data obtained under basal con-ditions, second specimen urine (1 hour) and first blood urea.

Second test (Fowweather's) is calculated from the fourth urine specimen (3 hours) i.e., post diuretic and the second blood specimen.

For those of you who are not familiar with this test, the clearance may be defined as "The volume of blood that could be completely cleared of urea by the kidneys

in 1 minute, if that were physiologically possible.''

A word about "standard" and "maximal" clearance. The excretion of urea is exactly proportional to the volume of urine secreted if the volume of urine secreted is over 2 ml. per minute. Under these circumstances we take 75 ml. of blood as the so-called 100 per cent maximal clearance.

When the volume of urine excreted is below 2 ml. the excretion of urea is proportional to the square root of the volume of urine excreted. Under these circumstances we take 54 ml. as the so-called 100 per cent standard clearance.

The standard and maximal clearance volumes apply to both the Van Slyke and Fowweather tests, but in the case of the Fowweather clearance the volume for normality is always taken as 75 ml. since it is reasoned that the diuretic effect of giving urea should normally increase the urinary output to maximal volumes.

In both Van Slyke and Fowweather clearance tests, clearance values above 75 per cent of normal are generally considered as satisfactory; between 50 and 75 per cent indicate mild deficiencies; and below 50 per cent severe renal damage.

I want now to turn to the picture presented by the toxaemias of pregnancy. First the mild case, which is commonly seen about the 25th week.

Here is the actual report on such a case:
CASE I. Aged 37 years; primigravida; 24 weeks pregnant. No significant medical history. Slight oedema for 3 weeks. Blood-pressure 156/100. Urine: albumin 0.025 mg./100.

FIG. 2.

RENAL FUNCTION TEST.

CASE I. Serial No. P. 47/45; 24 weeks pregnant, April 6th, 1945.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
4.30	295	1013	1.70	5.015	0.025
5.30	40	1014	1.40	0.560	0.025
6.30	64	1014	1.90	1.216	0.010
7.30	82	1013	2.50	2.050	0.010
8.30	70	1013	2.30	1.610	0.010

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 216 ml.

Weight of urea excreted in 3 hours after urea, 4.876 g.

Average urea concentration, 2.25 per cent.

Blood Specimens.

Blood urea before urea, 36 mg. per 100 ml.

Non-protein-nitrogen before urea, 36 mg. per 100 ml.

Blood urea after urea, 62 mg. per 100 ml.

Non-protein-nitrogen after urea, 47 mg. per 100 ml.

Urea Clearance Test before Urea (Van. Slyke).

Volume of urine, 40 ml. (Time, 60 minutes).

Volume of urine per minute, 0.67 ml.

Urinary urea, 1,400 mg. per 100 ml.

Blood urea, 36 mg. per 100 ml.

Standard clearance per minute,

$$1,400/36 \times \sqrt{0.67} \text{ ml.}$$
$$= 32 \text{ ml.,}$$
$$= 63 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 82 ml. (Time, 60 minutes).

Volume of urine per minute, 1.37 ml.

Urinary urea, 2,500 mg. per 100 ml.

Blood urea, 62 mg. per 100 ml.

Clearance per minute,

$$2,500/62 \times \sqrt{1.37} \text{ ml.}$$
$$= 47 \text{ ml.,}$$
$$= 63 \text{ per cent of normal.}$$

Note:

1. Slight delay in concentration (specific gravity).

2. Low total urea.

3. Slightly raised first blood values (within normal).

4. Raised second blood values indicating nitrogen-retention.

5. Both clearances indicate mild deficiency.

After 2 weeks' rest and treatment there was no oedema; blood-pressure 126/92.

FIG. 3.

RENAL FUNCTION TEST.

CASE I. Serial No. P. 112/45, 26 weeks pregnant, April 20th, 1945.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
4.30	314	1013	1.8	5.652	0.020
5.30	40	1013	1.4	0.560	0.020
6.30	68	1010	1.9	1.292	0.010
7.30	110	1016	2.3	2.530	0.010
8.30	86	1017	2.3	1.892	0.015

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 264 ml.

Weight of urea excreted in 3 hours after urea, 5.714 g.

Average urea concentration, 2.16 per cent.

Blood Specimens.

Blood urea before urea, 23 mg. per 100 ml.

Non-protein-nitrogen before urea, 21 mg. per 100 ml.

Blood urea after urea, 52 mg. per 100 ml.

Non-protein-nitrogen after urea, 42 mg. per 100 ml.

Urea clearance Test before Urea (Van Slyke).

Volume of urine, 40 ml. (Time, 60 minutes).

Volume of urine per minute, 0.67 ml.

Urinary urea, 1400 mg. per 100 ml.

Blood urea, 23 mg. per 100 ml.

Standard clearance per minute,

$$1400/23 \times \sqrt{0.67} \text{ ml.}$$

= 49.5 ml.,

= 92 per cent of normal.

Urea Clearance after Urea (Fowweather).

Volume of urine, 110 ml. (Time, 60 minutes).

Volume of urine per minute, 1.83 ml.

Urinary urea, 2300 mg. per 100 ml.

Blood urea, 52 mg. per 100 ml.

Clearance per minute,

$$2300/52 \times \sqrt{1.83} \text{ ml.}$$

= 60 ml.,

= 80 per cent of normal.

Note:

1. Water excretion increased.

2. Improved concentration (specific gravity).

3. Total urea approaching normal.

4. Low first blood values (low protein diet).

5. Very slightly raised second blood values.

6. Clearances improved.

This patient was kept under close supervision and remained well until the 32nd week, when there was a return of symptoms. Blood-pressure 150/108; Urine: albumin 0.05 mg./100; slight oedema of feet and sacrum.

FIG. 4.

RENAL FUNCTION TEST.

CASE I. Serial No. P.145/45, 32 weeks pregnant, June 15th, 1945.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
4.30	330	1015	1.5	4.950	0.1
5.30	47	1013	1.2	0.564	0.1
6.30	71	1012	1.7	1.207	0.1
7.30	86	1011	2.0	1.720	0.05
8.30	63	1012	2.2	1.386	0.1

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 220 ml.

Weight of urea excreted in 3 hours after urea, 4.313 g.

Average urea concentration, 1.96 per cent.

Blood Specimens.

Blood urea before urea, 23 mg. per 100 ml.

Non-protein-nitrogen before urea, 30 mg. per 100 ml.

Blood urea after urea, 41 mg. per 100 ml.

Non-protein-nitrogen after urea, 48 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 47 ml. (Time, 60 minutes).

Volume of urine per minute, 1.43 ml.

Urinary urea, 1200 mg. per 100 ml.

Blood urea, 23 mg. per 100 ml.

Standard clearance per minute,

$$1200/23 \times \sqrt{0.78} \text{ ml.}$$
$$= 46 \text{ ml.,}$$
$$= 85 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 86 ml. (Time, 60 minutes).

Volume of urine per minute, 1.43 ml.

Urinary urea, 2000 mg. per 100 ml.

Blood urea, 41 mg. per 100 ml.

Clearance per minute,

$$2000/41 \times \sqrt{1.43} \text{ ml.}$$
$$= 58.5 \text{ ml.,}$$
$$= 78 \text{ per cent of normal.}$$

Note:

1. Delay in concentration (specific gravity).

2. Low total urea.

3. Slight rise in second blood values but no obvious nitrogen-retention on clearance values.

Her condition did not improve despite treatment and her blood-pressure remained stationary at the raised level.

At 37 weeks: blood-pressure 156/108; headaches and visual disturbances; slight oedema of abdominal wall and legs.

FIG. 5.

KIDNEY FUNCTION TEST.

CASE 1. Serial No. P. 167/45, 37 weeks pregnant, July 19th, 1945.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
4.30	565	1004	0.90	5.085	0.05
5.30	42	1010	1.20	0.494	0.10
6.30	35	1010	1.80	0.630	0.15
7.30	47	1010	2.60	1.222	0.10
8.30	30	1012	2.40	0.720	0.10

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 112 ml.

Weight of urea excreted in 3 hours after urea, 2.572 ml.

Average urea concentration, 2.30 per cent.

Blood Specimens.

Blood urea before urea, 28 mg. per 100 ml.

Non-protein-nitrogen before urea, 30 mg. per 100 ml.

Blood urea after urea, 57 mg. per 100 ml.

Non-protein-nitrogen after urea, 49 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 42 ml. (Time, 60 minutes).

Volume of urine per minute, 0.70 ml.

Urinary urea, 1200 mg. per 100 ml.

Blood urea, 28 mg. per 100 ml.

Standard Clearance per minute,

$$1200/28 \times \sqrt{0.70} \text{ ml.}$$
$$= 36 \text{ ml.,}$$
$$= 67 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 47 ml. (Time, 60 minutes).

Volume of urine per minute, 0.78 ml.

Urinary urea, 2600 mg. per 100 ml.

Blood urea, 57 mg. per 100 ml.

Clearance per minute,

$$2600/57 \times \sqrt{0.78} \text{ ml.}$$
$$= 40.5 \text{ ml.,}$$
$$= 54 \text{ per cent of normal.}$$

Note:

1. Urinary volume diminished.
2. Total urea falling.
3. Second blood values rising.
4. Clearances falling.

This patient was induced at once and had a spontaneous delivery of a live female child.

It might appear at this stage that these rather elaborate tests yielded very little more information than could be gained in the ward. At first the patient responded obviously to treatment and later she did not, and the clinical picture told all that. The renal function tests merely confirmed this. That is indeed the general impression gained from tests carried out in the antenatal period. Occasionally the renal function test anticipates the clinical picture of failure.

In addition to renal function tests done during pregnancy we have had the opportunity to follow up a considerable number of cases after delivery, and here I feel that the test gives a much clearer idea of the ultimate result of renal function than that shown by the general clinical picture.

To summarize these results I think that it may be said that one of three things may happen in renal function tests following toxaemia of pregnancy.

1. There may be a rapid return to normal function. This is relatively uncommon in my experience.

2. There may be a very prolonged period of renal deficiency. This I would like to call the post-toxaemic state. It may gradually revert to normal or may gradually merge into the third condition.

3. The secondary hypertensive state.

The pictures given by renal function tests are reasonably clear-cut in the last two conditions—the post-toxaemic and the secondary hypertensive state, and below are two figures (Nos. 6 and 7) illustrating these.

FIG. 6.

RENAL FUNCTION TEST.

Specimen of post-toxaemic state.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
Zero	186	1018	2.0	3.720	0.1
1.0 hour	27	1018	1.8	0.486	0.1
2.0 hours	60	1014	1.4	0.840	0.05
3.0 hours	78	1017	1.9	1.520	0.1
4.0 hours	44	1018	2.2	0.968	0.1

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 182 ml.

Weight of urea excreted in 3 hours after urea, 3.328 g.

Average urea concentration, 1.84 per cent.

Blood Specimens.

Blood urea before urea, 28 mg. per 100 ml.

Non-protein-nitrogen before urea, 26 mg. per 100 ml.

Blood urea after urea, 75 mg. per 100 ml.

Non-protein-nitrogen after urea, 55 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 27 ml. (Time, 60 minutes).

Volume of urine per minute, 0.45 ml.

Urinary urea, 1800 mg. per 100 ml.

Blood urea, 28 mg. per 100 ml.

Standard maximal clearance per minute,

$$1800/28 \times \sqrt{0.45} \text{ ml.}$$
$$=43 \text{ ml.,}$$
$$=80 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 78 ml. (Time, 60 minutes).

Volume of urine per minute, 1.30 ml.

Urinary urea, 1900 mg. per 100 ml.

Blood urea, 75 mg. per 100 ml.

Clearance per minute,

$$1900/75 \times \sqrt{1.30} \text{ ml.}$$
$$=29 \text{ ml.,}$$
$$=39 \text{ per cent of normal.}$$

Post-toxaemic State.

Note:

1. Good concentrating powers (specific gravity and urea percentage).

2. Persistence of moderate amount of albumin.

3. Low water-excretion.

4. Low total urea.

5. Normal first blood values.

6. Good (Van Slyke) clearance under basal conditions.

8. Poor (Fowweather) clearance �️ Nitrogen-

7. Raised second blood values. ⎬ retention under load.

This might be termed a " low reserve kidney " associated with albuminuria.

Secondary Hypertensive State.

FIG. 7.
RENAL FUNCTION TEST.

Specimen of secondary hypertensive state.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
Zero	420	1018	1.0	4.20	Trace
1	70	1014	0.8	0.56	Trace
2	110	1009	1.4	1.54	Trace
3	110	1010	1.4	1.54	Trace
4	90	1010	1.5	1.35	Trace

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 310 ml.

Weight of urea excreted in 3 hours after urea, 4.43 g.

Average urea concentration, 1.42 per cent.

Blood Specimens.

Blood urea before urea, 38 mg. per 100 ml.

Non-protein-nitrogen before urea, 35 mg. per 100 ml.

Blood urea after urea, 60 mg. per 100 ml.

Non-protein-nitrogen after urea, 52 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 70 ml. (Time, 60 minutes).

Volume of urine per minute, 1.17 ml.

Urinary urea, 800 mg. per 100 ml.

Blood urea, 38 mg. per 100 ml.

Standard maximal clearance per minute,

$$800/38 \times \sqrt{1.17} \text{ ml.,}$$
$$= 23 \text{ ml.,}$$
$$= 42 \text{ per cent of normal.}$$

Urea clearance after Urea (Fowweather).

Volume of urine, 110 ml. (Time, 60 minutes).

Volume of urine per minute, 1.83 ml.

Urinary urea, 1400 mg. per 100 ml.

Blood urea, 60 mg. per 100 ml.

Clearance per minute,

$$1400/60 \times \sqrt{1.83} \text{ ml.}$$
$$= 31.5 \text{ ml.,}$$
$$= 42 \text{ per cent of normal.}$$

Note:

1. Delayed or impaired concentrating powers; specific gravity and urea percentage.

2. Low total urea.

3. Normal or high water-excretion.

4. First blood values at upper limit of normal.

5. High second blood values.

6. Low clearances; both approximately the same.

7. Obvious nitrogen-retention under load.

I think that the following case illustrates well this slow translation from the post-toxaemic to the secondary hypertensive state.

CASE 2. The patient was a woman aged 31; 2 previous normal pregnancies.

Third Pregnancy.

25th week. Attended hospital with toxaemia; blood-pressure 130/80; slight albuminuria.

27th week. After rest at home; headaches; blood-pressure 144/104.

27th to 32nd weeks. Felt well; no oedema; slow rise of blood-pressure to 150/108.

33rd week. Swelling of hands and feet; blood-pressure risen to 192/118; admitted to hospital.

34th week. Felt well; oedema subsiding somewhat; blood-pressure 160/118.

35th week. Allowed out of bed; blood-pressure immediately rose to 190/118. Three days later the blood-pressure was 200/120.

The membranes were ruptured with a Drew-Smythe catheter. On the following day an assisted breech delivery of a live premature female child was followed 20 minutes after by a single eclamptic fit.

1 day postpartum, blood-pressure 200/120.

1 week postpartum, blood-pressure 160/120.

2 weeks, the patient felt well and was sent home. Blood-pressure 160/120.

4th week. Headaches and dimness of vision. Blood-pressure 198/126.

13th week. Symptoms persist; blood-pressure 184/112.

21st week. Symptoms persist; blood-pressure 186/116.

A renal function test was then done and is shown in Fig. 8.

FIG. 8.

RENAL FUNCTION TEST.

CASE 2. Serial No. 646/43; 21 weeks postpartum.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
6.50	202	1018	1.8	3.636	0.12
7.50	64	1014	1.1	0.704	0.05
9.00	134	1009	1.1	1.474	0.02
10.00	76	1013	2.0	1.520	0.03
11.05	57	1015	2.2	1.144	0.05

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 250 ml.

Weight of urea excreted in 3 hours after urea, 3.918 g.

Average urea concentration, 1.56 per cent.

Blood Specimens.

Blood urea before urea, 34 mg. per 100 ml.

Non-protein-nitrogen before urea, 26 mg. per 100 ml.

Blood urea after urea, 68 mg. per 100 ml.

Non-protein-nitrogen after urea, 48 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke)

Volume of urine, 64 ml. (Time, 60 minutes).

Volume of urine per minute, 1.07 ml.

Urinary urea, 1100 mg. per 100 ml.

Blood urea, 34 mg. per 100 ml.

Standard maximal clearance per minute,

$$1100/34 \times \sqrt{1.07} \text{ ml.}$$
$$= 33.3 \text{ ml.,}$$
$$= 62 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 76 ml. (Time, 60 minutes).

Volume of urine per minute, 1.27 ml.

Urinary urea, 2000 mg. per 100 ml.

Blood urea, 68 mg. per 100 ml.

Clearance per minute,

$$2000/68 \times \sqrt{1.27} \text{ ml.}$$
$$= 33.2 \text{ ml.}$$
$$= 44 \text{ per cent of normal.}$$

Note:

1. Moderate albuminuria.

2. Low total urea.

3. Normal first blood values.

4. Raised second blood values.

5. Poor second clearance.

Indicative of post-toxaemic state.

At the 45th week the renal function test was repeated; blood-pressure 176/112 and Fig. 9 shows the beginning of the change from the post-toxaemic to the secondary hypertensive state.

FIG. 9.

RENAL FUNCTION TEST.

CASE 2. Serial No. 2002/43: 45 weeks postpartum: September 28th, 1943.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
5.0	408	1011	1.20	4.896	Nil
6.0	89	1012	1.30	1.157	Nil
7.0	188	1009	1.05	1.974	Nil
8.0	106	1012	1.70	1.802	Nil
9.0	72	1014	1.73	1.246	Nil

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 366 ml.

Weight of urea excreted in 3 hours after urea, 5.022 g.

Average urea concentration, 1.37 per cent.

Blood Specimens.

Blood urea before urea, 41 mg. per 100 ml.

Non-protein-nitrogen before urea, 35 mg. per 100 ml.

Blood urea after urea, 83 mg. per 100 ml.

Non-protein-nitrogen after urea, 54 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 89 ml. (Time, 60 minutes).

Volume of urine per minute, 1.48 ml.

Urinary urea, 1300 mg. per 100 ml.

Blood urea, 41 mg. per 100 ml.

Standard maximal clearance per minute,

$$1300/41 \times \sqrt{1.48} \text{ ml.}$$
$$= 38.5 \text{ ml.,}$$
$$= 71.3 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 106 ml. (Time, 60 minutes).

Volume of urine per minute, 1.76 ml.

Urinary urea, 1700 mg. per 100 ml.

Blood urea, 83 mg. per 100 ml.

Clearance per minute,

$$1700/83 \times \sqrt{1.76} \text{ ml.}$$
$$= 27.2 \text{ ml.,}$$
$$= 36.3 \text{ per cent of normal.}$$

Note :

1. Absence of Albumin ? Disappearance of old tubular damage.

2. Increased water-excretion.

3. Improvement in urea total.

4. Good clearance under basal conditions.

5. Poor clearance and nitrogen-retention under load.

After this the blood-pressure steadily mounted to the region of 200/130-40. The next renal function test was done 84 weeks post-partum.

Here the picture of secondary hypertension is nearly complete.

FIG. 10.

RENAL FUNCTION TEST.

CASE 2. Serial No. 1499/44; 84 weeks post-partum; June 27th, 1944.

Urinary Specimens.

Time	Volume (ml.)	Specific gravity	Urea (percentage)	Urea, Total (g.)	Albumin (percentage)
5.0	205	1018	1.2	2.460	0.01
6.0	80	1018	1.2	0.960	0.01
7.0	70	1010	1.2	0.840	Trace
8.0	156	1011	1.4	2.184	Trace
9.0	90	1013	1.6	1.440	Trace

Urea Concentration Test.

Volume of urine secreted in 3 hours after urea, 316 ml.

Weight of urea excreted in 3 hours after urea, 4.464 g.

Average urea concentration, 1.41 per cent.

Blood Specimens.

Blood urea before urea, 46 mg. per 100 ml.

Non-protein-nitrogen before urea, 32 mg. per 100 ml.

Blood urea after urea, 86 mg. per 100 ml.

Non-protein-nitrogen after urea, 55 mg. per 100 ml.

Urea Clearance Test before Urea (Van Slyke).

Volume of urine, 80 ml. (Time, 60 minutes).

Volume of urine per minute, 1.33 ml.

Urinary urea, 1200 mg. per 100 ml.

Blood urea, 46 mg. per 100 ml.

Standard maximal clearance per minute,

$$1200/46 \times \sqrt{1.33} \text{ ml.}$$
$$= 30 \text{ ml.,}$$
$$= 55.5 \text{ per cent of normal.}$$

Urea Clearance after Urea (Fowweather).

Volume of urine, 156 ml. (Time, 60 minutes).

Volume of urine per minute, 2.6 ml.

Urinary urea, 1400 mg. per 100 ml.

Blood urea, 86 mg. per 100 ml.

Clearance per minute,

$$1400/86 \times \sqrt{2.6} \text{ ml.}$$
$$= 42.3 \text{ ml.,}$$
$$= 56.4 \text{ per cent of normal.}$$

Note:

1. Delay in concentrating (specific gravity and urea percentage).
2. Low total urea.
3. Slightly raised water excretion.
4. Rather high first blood values.
5. High second blood values.
6. Low clearances approximating to the same value.
7. Obvious nitrogen-retention.

It is premature at this stage to dogmatize upon the conclusions one draws whilst seeing so many of these tests. But it is inevitable that one gathers impressions as one goes along I think that these may be summarized briefly.

1. The post-toxaemic state is a real condition and not merely something that exists in a laboratory report.

2. The duration of this state is longer than is generally thought. So far as the cases that I have seen show, it seldom lasts less than 7 months and is usually detectable up to a year.

3. The factors which decide whether the patient makes a good recovery from this condition or passes on to the secondary hypertensive state are probably multitudinous. Possibly the 2 most important are:

(*a*) The amount of rest that the patient can get during the first few months after delivery. War and post-war conditions obviously do not help the unfortunate mothers in this respect. This imponderable aspect will not, therefore, be discussed further.

(*b*) The duration of raised blood-pressure due to the pregnancy toxaemia.

Secondary hypertensive changes following the post-toxaemic state seem to occur far more frequently in those cases where the blood-pressure has remained high and pregnancy allowed to continue in the hope of getting at least one live baby for the anxious mother. The length of time during which the blood-pressure remains high seems to be a far more important factor than the very great heights to which it may rise. The late toxaemic with a very high blood-pressure, culminating possibly in eclampsia may have a prolonged post-toxaemic state, but rarely develops secondary hypertensive changes.

I feel that one must consider this post-toxaemic state more seriously, and it seems to me that there are 2 possible approaches to the problem.

First, in the matter of prevention, one may have to become rather more critical and stringent in the assessment as to whether a patient with toxaemia should be allowed to continue her pregnancy.

Secondly, as to treatment, the possible development of secondary hypertension, approximating as it does in function to chronic nephritis, offers a serious menace to the mother's future health. Whereas there are reasonably adequate facilities for the hospitalization of the pregnant toxaemic, such are almost entirely lacking for the post-toxaemic. To the woman who takes her responsibilities as a housewife and as a mother with any seriousness, the first few months following delivery are very busy and certainly do not provide conditions to promote a fall in blood-pressure. There, therefore, seems to be a very good case for the provision of beds, possibly in a convalescent home, with facilities for the routine check of the post-toxaemic woman and her child, and possibly this lightening of domestic responsibilities would do much to reduce the incidence of the secondary hypertensive state.

In conclusion I would like to express my indebtedness to the medical staff of the Jessop Hospital for Women, from whose case-records I have widely and indiscriminately abstracted the material for this paper.

Riboflavin Deficiency in Pregnancy
Its Relationship to the Course of Pregnancy and to the Condition of the Foetus.

BY

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During the past few years considerable attention has been paid to the relation between prenatal malnutrition on the one hand and the complications of pregnancy, labour and the puerperium and the condition of the, foetus at birth on the other hand. In these studies it has been shown that pregnancy in women on poor diets is frequently accompanied by obstetrical complications, such as miscarriages, still-births and premature deliveries (Ebbs, Tisdall and Scott, 1941; Burke *et al.*, 1943; Burke, Harding and Stuart, 1943a; Stuart, 1945). It has also been claimed that the birth-weight of the infant and its development up to 6 months are influenced by the prenatal nutritional state of the mother (Ebbs, Tisdall and Scott, 1941; Stuart, 1945; Burke, Harding and Stuart, 1943b). The results of large scale investigations, such as those described in the Interim Report of the Peoples' League of Health (1942) in England on 5,022 expectant mothers and those reported by Balfour (1944) on 11,618 pregnant women have also provided evidence as to the harmful effect of malnutrition on the course of pregnancy and the condition of the foetus. Although the influence of diets deficient in calories and various essential nutrients seems to be established, there is insufficient knowledge as to the effect of individual vitamin deficiencies on the pregnant woman and on the newborn child.

During the war years in this country an opportunity to study the clinical syndrome of riboflavin deficiency arose (Dostrowski and Sachers, 1942; Braun, Bromberg and Brzezinski, 1943). This deficiency was especially frequent in pregnant women, and its peculiar clinical manifestations were described in a previous paper (Braun, Bromberg and Brzezinski, 1945). Generally the ariboflavinosis in these women was not accompanied by other deficiency diseases. Furthermore, close relationship was demonstrated between the riboflavin content of the diet, the clinical syndrome and the riboflavin excretion in the urine.

In the present paper the effect of riboflavin deficiency on the course of pregnancy and parturition, as well as upon the condition of the foetus at birth and its further development, is reported. The diagnosis of riboflavin deficiency in this study was based mainly on the amount of riboflavin excreted in the urine.

MATERIAL.

Three hundred and twenty-six women attending the prenatal clinic of the Rothschild-Hadassah University Hospital were studied. In this series the amount of ribo-

flavin in the morning urine was examined twice monthly and at least 6 times throughout pregnancy. According to the average amount of riboflavin excreted in the morning urine, this series was divided into 4 groups:

Group A, up to 100 g. per litre   60 cases
Group B, 100 g. to 200 g. per litre 62 cases
Group C, 200 g. to 300 g. per litre 123 cases
Group D, more than 300 g. per litre 81 cases
                                            ――――――
                                            325 cases

Two hundred and fifty to 500 g. of riboflavin per litre of urine should be considered as the average amount excreted by normal individuals in Palestine (Bavly, 1943).

In all our patients a complete physical and obstetrical examination was performed and a dietary history obtained. Data were

I. *Course of Pregnancy.*

Pre-eclamptic toxaemia. It has been assumed that toxaemia frequently arises in undernourished pregnant women (Ebbs, Tisdall and Scott, 1941; Brzezinski, Bromberg and Halevi, 1943). This could not be confirmed in our patients suffering from riboflavin deficiency (Table I). The incidence of toxaemia was low in groups A and B. Only 2 women had a slight elevation of blood-pressure during the last month of pregnancy and only 1 of them had albuminuria. On the other hand, in groups C and D 13 patients suffered from pre-eclamptic toxaemia. Three of them had severe forms of toxaemia with high blood-pressure, albuminuria and hypertensive changes in the optic fundi.

TABLE I.
Maternal Complications.

Cases	Patients							
	Group A.		Group B.		Group C.		Group D.	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Toxaemia of pregnancy	1	1.6	1	1.6	7	5.7	6	7.4
Vomiting and nausea	20	33.3	15	24.2	8	6.5	5	6.4
Prematurity	10	16.4	8	12.7	7	5.7	4	4.8
Hypogalactia	20	33.3	15	24.2	7	5.7	5	6.2
Agalactia	4	6.6	2	3.2	—	—	—	—

collected as to the social, economic and nutritional status of the patient and her family. The patients were re-examined at least once monthly, when the blood-pressure was taken and the urine examined for albumen. All these patients were delivered in our department and were observed during delivery and in the post-partum period; the newborn children were observed from birth until the age of 6 months.

In the 4 groups the influence of riboflavin deficiency on the course of pregnancy, labour, the postpartum period, lactation, foetal and neonatal mortality and the condition of the foetus at birth and its subsequent development, was investigated.

Vomiting. In groups A and B in which riboflavin urinary excretion was low, nausea and vomiting were very frequent. In group A there were 20 cases (33.3 per cent), in group B, 15 cases (24.2 per cent), while in groups C and D there were 8 and 5 cases respectively (6.5 and 6.4 per cent) (Table I). This hyperemesis, which occurred in the first 2 groups, almost always in the second half of pregnancy, was accompanied by heartburn and should not be considered at a manifestation of toxaemia but rather as being caused by anatomical changes in the pharynx and in the oesophagus due to riboflavin deficiency (Braun, Bromberg and Brzezinski, 1945).

Premature deliveries. Riboflavin defici-

ency seems to play an important role in the premature termination of pregnancy. In group A 10 cases of prematurity (16.4 per cent) occurred; in group B, 8 cases (12.7 per cent), in group C, 7 cases (5.7 per cent) and in group D, 4 cases (4.8 per cent) only (Table I). The number of premature deliveries in the first 2 groups is strikingly higher than that observed in our obstetrical clinics (Brzezinski, Bromberg and Halevi, 1943).

The frequency of other complications such as infections, haemorrhages, etc., was unaffected in the various groups.

II. *Course of Labour.*

No significant differences in respect to labour were found in the 4 groups studied. The incidence of haemorrhages and of instrumental deliveries was equally low in all groups. Since the percentage of primiparae and multiparae was approximately the same in the various groups, this factor does not influence the result of the investigation.

III. *Course of the Postpartum Period.*

In the postpartum period no major complications were observed in our patients: neither was any significant difference noted between the various groups in the frequency of mild infectious complications. The morbidity (including all cases which showed a rise of temperature over 38°C. for 2 days or more during the postpartum period) was equally low in all 4 groups: 8.3 per cent in group A; 8 per cent in group B; 6.6 per cent in group C, and 8.6 per cent in group D.

IV. *Lactation.*

With regard to the amount of milk secreted during the immediate postpartum period as well as the 6 first months following delivery, significant differences were observed between the various groups. In the first group (A) there were 20 cases of hypogalactia, an average amount of 200 g. milk had to be added after each meal. In the same group there were 4 cases of complete agalactia. In the second group (B) there were 13 cases of hypogalactia and 2 of agalactia. In the third group (C) 7 cases, and in the fourth group (D) 5 cases of hypogalactia were noted (Table I).

V. *Condition of the Foetus at Birth and its Subsequent Development.*

The condition of the foetus at birth seems not to be influenced by riboflavin deficiency. The average weight of the newborn at term was nearly the same in all 4 groups. However, the newborn of the first 2 groups (A and B) showed a definite tendency to gain less weight during the first weeks than those of the other control groups. This may be attributed to the artificial feeding which became necessary because of the hypogalactia of the mother in the groups with lower riboflavin excretion. The further development of the infants was also investigated. There were no significant differences during the 6 months following delivery in the 4 groups studied. All infants investigated were observed at the centre for infant care of the Hadassah University Hospital. It appears, therefore, that the antenatal riboflavin deficiency of the mother does not influence the development of the foetus.

VI. *Foetal Mortality.*

Antenatal death. The first 2 groups (A and B) showed a high percentage of foetal mortality during pregnancy. There were 3 cases in group A, 1 in the fifth and 2 in the eighth month. In these cases macerated foetuses were spontaneously expelled. In group B there were 3 cases of macerated foetuses, 1 in the eighth and 2 in the ninth month (Table II). In groups C and D there were no cases of macerated foetuses. It

should be stressed that in all cases of antenatal death of the foetus other causes such as diabetes, syphilis and toxaemia of pregnancy were excluded.

Intranatal death. One infant of group A died of cerebral haemorrhage due to difficulties in delivery.

Postnatal death. During the immediate postpartum period (first 2 weeks) 2 deaths occurred in group A due to prematurity of the infants. Both of them had had very low birth-weights (1600 g. and 1800 g.). One infant in group C died 3 hours after delivery because of asphyxia, and the second child after 4 days of bronchopneumonia (Table II).

to observe a series of pregnant women who had a very low riboflavin intake and presented clinical manifestations of ariboflavinosis. This deficiency was confirmed by the low urinary excretion of riboflavin. The purpose of our investigation was to establish the effect of riboflavin deficiency on the course of pregnancy, labour and on the condition of the foetus. We have not been able to observe any effect of riboflavin deficiency on the frequency of toxaemia, infections and haemorrhagic complications, although numerous authors have emphasized the high incidence of these complications in various nutritional deficiencies. On the other hand, vomiting was

TABLE II.
Foetal Mortality

Cases	Group A. No.	Group A. Per cent	Group B. No.	Group B. Per cent	Group C. No.	Group C. Per cent	Group D. No.	Group D. Per cent
Antenatal mortality	3	5.0	3	5.8	–	–	–	–
Natal mortality	1	1.7	–	–	–	–	–	–
Postnatal mortality	2	3.3	–	–	1	0.8	1	1.1

COMMENT.

It has been demonstrated in animals that lack of riboflavin in the food may lead to relative sterility and when reproduction was possible, to resorption of the product of conception (Warkany and Schraffenberger, 1944). Evidence is also available that riboflavin deficiency may cause congenital anomalies of the offspring (Warkany and Schraffenberger, 1943; Johnson, *et al.*, 1945). Since diets consumed by human beings are never completely riboflavin free, similar conditions as those observed in the above-mentioned experiments apparently do not occur in man. Therefore, the demonstration of the influence of riboflavin deficiency on the course of pregnancy and foetal development in man is more difficult than under experimental conditions. However, it was possible in this study

definitely prevalent in the groups with low urinary riboflavin excretion, probably because of anatomical changes in the upper digestive tract which accompanied the deficiency state.

A significant relationship was found to exist between riboflavin deficiency and the incidence of prematurity. The average incidence of premature deliveries in the groups with low riboflavin excretion was 14.6 per cent, while in the 2 remaining groups it was only 5.5 per cent. Very significant results were also obtained regarding the incidence of stillbirth due to antenatal death of the foetus. In the first 2 groups antenatal death occurred in 4.9 per cent of the cases; while in the other groups there was none at all. It appears also that riboflavin deficiency has a harmful effect on lactation. In group A 33.3

D

per cent of the cases had hypogalactia and in 6.6 per cent there was complete agalactia. In group B 25.5 per cent had hypogalactia while in group C and group D an average of only 5.9 per cent was noted.

SUMMARY.

1. A series of 326 pregnant women was divided into 4 groups according to the amount of riboflavin excreted in the urine.

2. There was no significant difference between the groups in the incidence of toxaemia of pregnancy, or of haemorrhagic and infectious complications during pregnancy, labour and the postpartum period.

3. A significant relationship was found between low riboflavin excretion in the urine and the following complications:

Vomiting (during the second half of pregnancy), prematurity, antenatal death of the foetuses, hypogalactia and agalactia.

4. Riboflavin deficiency in the mothers had no harmful effect on the birth weight of the infants or their further development.

ACKNOWLEDGMENTS.

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Some Factors Causing Difficult Labour in Multigravidae.*

BY

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ATTENTION has been called to the complications which may arise in labour in multigravidae by several authors, and in particular by Robinson (1930), who has written about " The Old Multipara ", and by Solomons (1934), who has described " The Dangerous Multipara ". These complications may be all the more difficult to surmount because they are often unexpected, and some major catastrophe, such as a rupture of the uterus, or some difficult operation, such as a high craniotomy, may terminate the labour. When difficult or obstructed labour occurs in a patient after a long history of normal deliveries, its explanation is often puzzling, and a series of cases has therefore been investigated in order to determine the factors responsible.

The tables of the obstetric abnormalities and the maternal deaths at Walton Hospital for the years 1936 to 1945 inclusive, have been searched. During this time there were just under 30,000 deliveries. The case histories of all patients who had had a difficult labour in the 8th or in any subsequent pregnancy after a previously normal obstetrical history have been reviewed, with the main object of determining the factors responsible for the gradual or sudden onset of such difficulty. The previous obstetrical history has not been considered abnormal, however, if there was an instrumental delivery in the first labour, if there were occasional instrumental deliveries or stillbirths at home, or if there were diffi-

cult labours terminating the 2 or 3 pregnancies prior to the one under consideration. After the 8th pregnancy, according to Kerr (1933), the mortality equals or exceeds that in the primigravida, and in the 10th pregnancy, according to Solomons, the mortality is 5 times that of all women in pregnancy.

It was found that transverse lie with its complications of prolapse of the cord and limbs was a common source of difficulty, and as the explanation of this is usually to be found in the laxity of the abdominal wall after many pregnancies, these cases have not been considered further. In some of these cases, however, the other factors which will be mentioned later are doubtless operative as well. Cases of antepartum haemorrhage have also been excluded, together with those in which difficulty was due to foetal monsters or cervical stenosis from previous amputation of the cervix.

After the exclusion of these cases, there were found to be 23 patients in whom there was serious difficulty in labour after a previously normal obstetrical history, and who merit the description of " dangerous multigravidae ". This incidence of only 23 cases among nearly 30,000 deliveries is a small one. Nevertheless these cases are worthy of consideration for several reasons. The maternal risk is high, and there were 3 maternal deaths and 2 cases of rupture of the uterus. Most of the patients needed some form of major interference. The factors responsible for the difficulty in these cases will also be found, to a less marked degree, in other patients

who have had fewer pregnancies, and this is a matter of some importance at the present moment, when it is very common to have to deal with patients who are pregnant again after a gap of many years. There must also be many other similar cases, which do not figure in tables of abnormalities, in which labour has been long, and perhaps to the patient difficult, but in which spontaneous delivery occurs. Finally, for reasons which will be discussed later, it is probable that this type of case will become rare with the passage of time, and is therefore worthy of consideration while it still confronts us in a formidable manner.

Clinical features. An attempt has been made to follow-up and examine clinically and radiologically all the cases seen in the more recent years of the period, but this was not successful, owing, no doubt, to the disturbance of the war and air raids, and to the heavy family responsibilities of these patients. Only 8 patients attended for further examination.

The average age of all patients was 40. Eleven patients under 40, and 12 patients over 40, 2 of them being 47. These patients, therefore, run both the risks of age and multiparity. The average number of pregnancies in 22 of the patients was 10, though this is probably an underestimate, as some patients with a long obstetrical history become a little forgetful about some of their pregnancies. Four patients had had 12 or more pregnancies. Some difficulty, indeed, has been found in obtaining an accurate obstetrical history from the records, as in many cases the previous labours had been at home and the details were vague. Moreover, the histories had often been recorded soon after the patients had been admitted with obstructed labour, and at a time when they were in great distress.

There were 12 Caesarean sections, 5 forceps deliveries, 2 craniotomies, 2 difficult breech deliveries, and 2 normal deliveries. In most of the cases delivered by Caesarean section the head was above the brim, and there were 2 high forceps deliveries. There were also 2 failed forceps cases, and 2 cases in which there was great difficulty with the delivery of the shoulders.

It is convenient to analyse the factors responsible for these difficult labours by considering respectively the powers, passages and passenger.

Powers. Much stress has been laid on inertia as a factor in slow or difficult labour in multigravidae, and fibrosis in the uterine muscle or shortage of calcium have been considered to be important factors. Assessment of the strength of the powers is always a matter of great difficulty, even when graphic methods are used. It is especially difficult from the mere consideration of case histories, or when the patient has not been seen throughout the whole labour. The strength and frequency of the pains may be judged from the patient's or observer's description of them. They may be judged from their effect on the foetus, the size of the caput, the amount of moulding or overriding, and the signs of foetal distress. It must be remembered, however, that when the cervix dilates up quickly, as it usually does in multigravidae, and the head is high, little caput may form, and there may be little moulding in a large well-ossified head. Finally, the occurrence of a ring or of rupture of the uterus may be looked upon as evidence of excessive uterine activity, excepting, of course, those cases of the silent rupture of an old scar.

It was found that in 15 of these cases there was evidence of strong uterine action as indicated by one or more of the standards just described. In the other 8 cases, the information was inadequate to justify the drawing of any conclusion about the matter. According to the available evidence, therefore, the factor of inertia does not seem to

have been an important one in causing difficult labour. It is true that secondary inertia does often occur in these patients, but this must be looked upon as the breathing space which Nature gives to the patient for rest and to the attendant for taking appropriate action before some major complication occurs. In the words of Leyland Robinson "Unhappily the case may be recognized as a type of primary inertia and treated along expectant lines . . ."

Passages. Bony pelvis. The dimensions of the bony pelvis have been investigated by clinical and radiological methods, and also by measurement of the true conjugate of the brim at Caesarean section or post-mortem examination. The results of clinical examination vary greatly with the personal factor, and in some cases there was disagreement between the findings of different observers. It is the rule in these multigravidae, however, to find that the pelvis can be explored with ease owing to the laxity of the soft tissues and the deficiency of the perineum, but at the same time this ease of examination may give a false idea of pelvic size, and this also applies to examination under anaesthesia.

In 9 cases there was clinical evidence of a small inlet or cavity. In 5 of these cases X-ray examination was carried out, and the radiological supported the clinical findings. In 1 case at Caesarean section, the true conjugate was estimated to be only 3 inches, and in another, at post-mortem examination, it was found to be 4 inches. In 1 case the pelvis seemed to be normal, and in the other 11 cases the clinical evidence was too incomplete for any conclusions to be drawn. Six patients were found to have a lumbar lordosis, and the significance of this will be discussed later. Two patients were described as having low symphyses. No cases of bony outlet contraction were found, and clinically

outlet obstruction did not occur, apart from difficulty with the shoulders of big babies.

Radiological investigation of the pelvis is now widely used, and whatever its scope in practice may be, it is generally agreed that it gives us an accurate idea of pelvic size and shape. For the reasons already mentioned, this method of examination was only possible in 8 cases. Three other cases had been X-rayed after delivery some years ago, but as the films were not available for study it has been thought wiser to disregard the findings. A picture of the brim by the Roberts method was taken, and also a lateral one. Outlet films were not as a rule taken, as this method is less reliable, and also because outlet difficulty was not a feature in these cases. A study was made of the antero-posterior and transverse measurements of the brim, the shape of the brim, the appearance of the coccyx and sacrum, and of the angles made by the plane of the pelvic brim with that of the anterior surface of the 5th lumbar vertebra and that of the upper part of the sacrum, as described by Malpas and Hamilton (1939).

Consideration of the measurements of the true conjugate taken in the Roberts films shows that, using the commonly accepted limits, there was 1 case with normal measurements (over $4\frac{1}{4}$ inches), 3 cases of slight contraction ($3\frac{3}{4}$ inches to $4\frac{1}{4}$ inches), 2 cases of moderate contraction ($3\frac{1}{4}$ inches to $3\frac{3}{4}$ inches), and 2 cases of severe contraction (below $3\frac{1}{4}$ inches). Ince and Young (1940) in their radiological study of over 500 pelves in London found no cases of severe contraction, and only 6 cases of moderate contraction. Their measurements, however, were of the obstetric true conjugate, measured in lateral films. The pelves in my series were flattened, the brim index in all cases being below 90, in 3 cases between 70 and 80, and in 1 case below 70. The brim areas were all

below the average found by Ince and Young, and in 5 out of 8 cases below their minimum. A simple method of estimating the pelvic capacity has recently been suggested by Weinberg and Scadron (1946). These authors found that if the sum of the antero-posterior and transverse diameters was less than 23 cm. dystocia was likely. By this standard 6 out of 8 brims measured were found to be small.

The important question of the shape of the pelvis will be discussed later. The average of the angles formed in 7 cases by the pelvic brim and the anterior surface of the 5th lumbar vertebra was found to be 127°, which compares with an average found by Malpas and Hamilton of 136°. The average of the angle formed in 7 cases of the pelvic brim and the first part of the sacrum was found to be 110°. This compares with an average of 100° in 19 other films examined, largely of abnormal pelves, and with an angle of 93° which was found by Ince and Young, their measurement being taken to the deepest part of the sacrum.

Consideration has been given to the possibility that either abnormalities of the pelvic joints or obstruction from the soft tissues might have been causes of difficult labour. It is said that with middle age there is gradual obliteration of the sacro-iliac joints. If this occurs it would limit pelvic expansion during pregnancy, and would also interfere with the alteration of pelvic diameters which follows rotation at the sacro-iliac joints. Unfortunately, it is very difficult to draw conclusions from either clinical or radiological examination of these joints, and it has been impossible to draw any conclusion about the matter beyond noting that no obvious abnormality was found. In 1 case in which a postmortem examination was made, the condition of the sacro-iliac joints seemed within normal limits.

No evidence of dystocia from soft-tissue obstruction was found. In some cases a swollen anterior lip of the cervix was a prominent feature, due doubtless to failure of the lower segment to retract over a high head. Cervical dystocia is rare in multigravidae, apart from those cases where scar tissue from a previous amputation or cauterisation of the cervix causes obstruction. Obstruction lower down in the genital tract is also rare, unless there is present vaginal stenosis from previous sepsis, or a perineorrhaphy has been carried out.

Passenger. The average weight of the babies was 8 pounds 15 ounces. There were 2 babies of 6 pounds, 4 of 7 pounds, 7 of 8 pounds, 5 of 9 pounds, 3 of 10 pounds, 1 of 11 pounds, and 1 of 12 pounds. The average weight is thus seen to be high, and the incidence of giant babies is considerable. In 2 cases there was great difficulty with the shoulders of babies weighing 10 pounds 11 ounces and 11 pounds 13 ounces respectively. Another patient had developed diabetes since her previous pregnancy, and Caesarean section for a baby weighing 12 pounds was required. An attempt was made to investigate the possibility that an increase of weight compared with that in previous pregnancies was a factor, but little accurate information was obtained about this, as in many cases the patients were vague about the matter, and also the alleged weight of babies born at home are notoriously inaccurate. In those cases in which a hospital record of previous weights was available, however, it was found that in 3 there was a definite increase in weight, of between 1 and 2 pounds, and in 3 others there was no increase.

Male babies were predominant, there being 17 of these as opposed to 6 females. Definite information about the actual date of delivery in relation to the expected date

was available in 9 cases: In 1 of these the patient was delivered before term, in 1 case at term, and in the other 15 cases at intervals ranging between 1 and 15 days after term.

There were 1 face and 1 brow presentation, both occurring in cases of contracted pelvis. There were 2 occipito-anterior positions, 4 occipito-posterior positions, 8 transverse heads, 1 breech presentation, and 2 transverse lies. In the other 4 cases the exact position was not noted.

DISCUSSION.

Consideration can now be given to determining the relative part played in the production of difficult labour by the factors which have been mentioned. The difficulties of assessing the strength of the powers have already been discussed, and these difficulties are all the greater when the patient has not been observed for the whole of the labour, but has been admitted as an emergency. Nevertheless, in no case in which adequate information was available did uterine action appear to be defective, according to the standards given. On the other hand, several patients were emphatic in saying, both at the time of the labour and subsequently, that not only were the pains excessive, compared with those of previous labours, but that they felt that even with very strong pains that a normal delivery would not take place.

In the case of the passages and the passenger, however, much more definite information is available, and measurements may be used for the purposes of comparison. In 5 cases the size of the baby seemed to be the important factor, the weights being 9 pounds 13 ounces, 10 pounds 6 ounces, 10 pounds 11 ounces, 11 pounds 13 ounces, and 12 pounds. In 7 cases the main factor responsible seemed to be a contracted pelvis, and in 5 of these X-ray pelvimetry was

carried out. In 5 more a small pelvis and a large baby were found, a large baby being here considered to be one of 9 pounds or more. In the remaining 6 patients, none of whom were followed up, there was no obvious cause of difficulty, except that in 2 of them there had been an increase in the weight of the baby compared with previous pregnancies.

The main factors are thus seen to be a small pelvis (12 cases) and a big baby (10 cases), and these findings support the views of Solomons. The incidence of contracted pelvis might have been found to be higher if it had been possible to follow up more of the cases.

There was some evidence, though this was not always detailed, in 10 of the cases that difficult labour was a progressive feature in the patient's obstetrical history, and in at least 7 of these there was pelvic contraction. What is the aetiology of this pelvic contraction?

The theory has been put forward by several authors that minor degrees of osteomalacia occur in this country and give rise to bony changes in the pelvis. Leyland Robinson states " . . . although true osteomalacia is rare in this country, there are minor grades of this disturbance which escape recognition." Browne (1942) states " . . . in the depressed industrial areas of England and Wales it is probable that minor degrees of this disease are more common than is generally supposed." MacLennan (1944), in reporting a recent case of osteomalacia in Glasgow, says " It is conceivable that some multiparous women in whom slight pelvic contraction is discovered for the first time in their later pregnancies may actually be suffering from a mild osteomalacia manifestation rather than the results of old-standing rachitic deformity." In spite of these views, however, there is little positive evidence about the occurrence of mild forms of osteo-

malacia. In India, Green-Armytage (1931) says " . . . in some women in this country minor degrees of osteomalacia may occur in the pelvic bones which obstruct labour." Dutta (1936) says that mild forms are common and difficult to diagnose, and that they may give rise to more trouble than established cases.

It is generally agreed that the severe forms of osteomalacia which occur in India and China and which have been described so excellently in the many writings of Preston Maxwell and Green-Armytage are rarely seen in this country. According to Bulmer (1935), only 12 cases had been recorded up to 1945. Kenny (1944) in the radiological examination of 1,000 pelves in London, found evidence of osteomalacia in only 1 patient, an Indian. MacLennan was able to find only 1 previous case in the records of the Glasgow Maternity Hospital in 30 years. I have been able to trace only 1 case which was admitted to the general wards of Walton Hospital in 10 years. It is unlikely that the extreme forms of this condition escape notice, owing to their marked clinical and radiological features. The evidence that the pelvic contraction in these cases now reported might have been due to a mild osteomalacia will be discussed from the radiological, clinical, biochemical and aetiological aspects, but it must be remembered that the certain diagnosis of this condition may provide great difficulty, and may not be possible without the histological examination of bone.

The *radiological* diagnosis may be made from the lack of density of bone, and from the bony deformities which are produced. The lack of density is relative, and diagnosis by means of this feature is difficult. There was no obvious change in the films examined, and it is probable that marked change only occurs in severe cases and is rapidly followed by bony deformity.

The classical bony deformity of the pelvis in osteomalacia is, of course, that of the " triradiate ", " rostrate ", " beaked ", or " three-cornered " pelvis, which is illustrated in the textbooks and found occasionally in the museums. Maxwell (1930) has detailed the changes in the pelvis, and among these are yielding at the acetabulum, approximation of the ischial tuberosities, and increased concavity of the sacrum with turning forward of the lower end. Osteoporosis in the region of the symphysis, a condition found by Young (1940) in pelvic osteo-arthropathy, has also been described in osteomalacia Little information is available about the early bony changes in the pelvis. Hess (1930), however, describes flattening of the pelvis from the forcing downwards and forwards of the sacral promontory, and other authors have described similar findings.

It has already been shown that flattening was a feature in the pelves examined radiologically, and that there was increased inclination of the sacrum, which in a few cases was marked. Associated with these changes clinically was a lumbar lordosis, a feature sometimes making the induction of spinal anaesthesia difficult, and occasionally also some tenderness over the sacrum. In 6 out of the 8 cases there was some prominence in the region of the acetabulum, or the pelvis was triangular, heart-shaped or android. In 6 cases there was marked curving of the lower sacrum.

The bony changes, therefore, are those which might be expected to occur in a softened pelvis from the transmission of weight through the acetabula, the iliopectineal lines, and the sacro-iliac joints to the vertebral column. They differ in degree from the extreme classical changes which are doubtless produced by crumpling occurring with great rapidity in a very softened pelvis, and are somewhat similar to those found in rickets. The original

shape of the pelvis must also affect the nature of the changes.

Clinically, the symptoms of osteo-malacia may be very variable, and Green-Armytage describes several clinical types. Important symptoms are those of back-ache and difficulty in walking. The Chinese name for this disease, according to Preston Maxwell, means " back and thigh pain." Four of the cases followed up had had backache in pregnancy. Other symptoms complained of were that the patient " couldn't walk ", " couldn't use her hands", "felt helpless", and was "weighed down". Vomiting and lack of appetite were common complaints. It is interesting to note that tenderness over the costal margins, which is a common complaint in multigravidae in this country, is, accord-ing to Preston' Maxwell, a symptom of osteomalacia.

Biochemical findings were not available in these cases, and, according to Preston Maxwell, the levels of serum calcium and phosphorus are not necessarily altered in this disease. In 1 recent case, not included in the present series, the serum calcium was 10.6 mg., and phosphorus 3.1 mg. per cent. In the case of osteomalacia in Walton Hospital mentioned above, the figures on several occasions were within normal limits.

The *aetiological* factors now believed to be responsible for the development of osteomalacia are deficiency of calcium, phosphorus and vitamin D in the diet, together with lack of sunlight. Preston Maxwell gives details of the diets of Chinese patients suffering from oestomalacia, and it seems probable that the diets formerly consumed by patients in the depressed in-dustrial areas of this country did not differ greatly from these in their lack of first-class protein, and calcium, phosphorus and Vitamin D, and in their relative excess of cereals. Browne quotes evidence about the

shortage of calcium in particular. An intake of 2 pints of milk daily is required to ensure an adequate supply of calcium, in addition to the consumption of other calcium con-taining foods. An attempt has been made to investigate this matter of diet in the patients who were followed-up. It proved difficult, however, to obtain information on this point. A mother will not admit that she starves herself in order to feed her other children, but it is the belief of health visitors who see these patients in their own homes that even now, when milk is more freely obtainable, patients drink very little them-selves during pregnancy, and before the war even less was consumed. One patient admitted that " she never drank milk ". Only recently, also, has administration of vitamins A and D become more general.

The economic circumstances of most of these patients were very bad, as their re-productive era had corresponded with a period of great industrial depression in Liverpool. The husband of 1 patient had been out of work for 10 years.

Among other factors investigated was the frequency of the pregnancies in these patients, and it was found that the average interval between pregnancies in cases in which details were available was less than 2 years. Details of lactation were only available in 4 cases, and in 3 of these it was prolonged.

It is interesting to speculate why osteo-malacia is so rare in places where rickets is so common, such as Glasgow, in view of their similar aetiology, and this matter has recently been discussed by MacLennan. In Central Europe after the 1914–18 War, hunger osteomalacia, as it was then called, was common under the same conditions which produced rickets. Trousseau (quoted by Bulmer) who first called osteo-malacia in 1868 the " rickets of adults ", said, " There exists, then, in pregnant women, a certain kind of rickets, of which

osteomalacia may be considered a more advanced degree." Possible explanations may be that the diets in this country are not quite so deficient in mineral salts and vitamins, or that intestinal infection is not so frequent or so severe as in India and China, or on the other hand that there is just sufficient sunshine, to help to prevent the condition, even in our northern industrial cities.

In the small number of patients which it has been possible to follow-up, evidence was found of pelvic contraction with changes similar to those which occur in the early stages of osteomalacia. Many of the patients had had symptoms in pregnancy similar to those suffered from by patients with osteomalacia, and their diets over many years had been deficient in those factors whose shortage is now believed to be mainly responsible for osteomalacia. Clinically, evidence was found that the pelvic contraction had developed late in the patient's obstetrical history, and its progressive nature in some cases was indicated by gradually increasing difficulty in labour. All this evidence seems to support the view advanced by the authors mentioned previously that a mild form of osteomalacia does occur in this country and produce pelvic contraction and difficult labour.

Even if these conclusions about the aetiology of these cases are not correct, there can be little doubt from the evidence presented that in some multigravidae after many normal confinements an often unexpected difficult or obstructed labour may arise, due to disproportion from a small pelvis or a large baby or both.

If osteomalacia is a factor in these cases, it might be held to explain the defective uterine action which is said to occur in these cases from shortage of calcium, but it is interesting to note that both Green-Armytage and Preston Maxwell have found that at Caesarean section in these cases the uterine contractions were very forceful.

The bearing of these findings on treatment may be briefly considered. The classical treatment in this type of multigravida with delayed labour and a high head has always been that of internal version. This may be very easy, owing to the laxity of the abdominal wall and the soft tissues. On the other hand, it must be remembered that these cases are often not seen, or at any rate recognized, till late in labour. In such cases the uterus may be dry, and rupture of the lower segment may occur very easily in these multigravidae. In 1 case in this series such a rupture followed the breech delivery of a large baby. Moreover, the breech extraction may be difficult on account of the disproportion which is present in most cases, and this may only become obvious when attempts are being made to deliver the after-coming head. The old operation of high forceps may occasionally be justifiable in expert hands. Once the head has passed through the brim, the rest of the delivery may be easy. The Kielland forceps is valuable, as the head is usually transversely arrested, and this instrument was used in 1 case in this series. It is advisable to apply the anterior blade by the wandering method, rather than by the classical method of turning it upside down in the lower segment.

Caesarean section is preferable in this type of case, and was the most frequent method of delivery in this series. Nevertheless, it must be borne in mind that these patients are not good subjects for abdominal operations, and especially for general anaesthesia, as the abdominal wall is often thick, pendulous and oedematous. The puerperium is usually stormy, and there was one case of burst abdomen, 2 cases of thrombo-phlebitis, and 1 ventral hernia. The findings of Green-Armytage in India

that in neglected cases of difficult labour a lower segment Caesarean section was safer than a craniotomy must always be remembered, and modern chemotherapy has probably still further decreased the risk of this method of delivery.

It is probable, however, that in time this type of case will become very rare with improved economic conditions, a falling birth-rate, and diets more adequate in quantity and quality.

CONCLUSIONS.

(1) A series is reviewed of 23 patients in whom difficult or obstructed labour occurred in their 8th or subsequent pregnancy after a previously normal obstetrical history.

(2) The main factors responsible for the difficulty were found to be a small pelvis and a large baby.

(3) Evidence is brought forward that the pelvic contraction is due to a mild form of osteomalacia.

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THOMAS WATTS EDEN, M.D.

The late Thomas Watts Eden, M.D., F.R.C.P., F.R.C.S., who, until his death on the 22nd September last, was Chairman of the Directors and of the Editorial Committee of the Journal, by his Will gave his Trustees two sums, each of £10,000, free of duty, to found, after the death of his widow, two "travelling" fellowships, the first to encourage the study of obstetrics and gynaecology, the second the study of infancy and early childhood in health and disease (paediatrics).

After the death of the widow these funds are to be transferred, one to the Royal College of Obstetricians and Gynaecologists and the other to the Royal College of Physicians, the President and senior officers of which are (with others) to be the judges in making the awards. Candidates must be graduates of either sex (whether members of the College concerned or not) of not less than 2 years standing of any approved University in the British Empire and Commonwealth.

Each fellowship is for a period not exceeding 3 years and the awards are to be made according to the academic progress of a candidate before graduating and his attainments during the postgraduate period, and will not be made by competitive examination.

After 10 years from the first award the conditions may be varied at the discretion of the judges.

Anuria Following Criminal Abortion

BY

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THE present communication deals with a case in which changes in the uterus resembling those found in the graver forms of concealed accidental haemorrhage ("uteroplacental apoplexy") were produced by the forcible injection into the birth passages of a mixture of soap and dettol in an effort to produce abortion. The case possesses special interest in that the massive uteroplacental injury so produced was followed rapidly by a breakdown in kidney function with oliguria, azotaemia and death.

CASE REPORT.

The patient was admitted to Hammersmith Hospital on March 16th, 1946. She was aged 31, single and nulliparous, and stated that her last menstrual period was on December 25th, 1945. Previously her cycle had been regular and of the 4/.28 day type. The following statement was obtained and was checked in its major details by reference to the abortionist and the patient's mother and fiancé. The patient attempted to procure abortion by repeated douching daily with soap and water over the preceding month in addition to taking calomel and "female pills". Being unsuccessful she made arrangements to visit an abortionist on March 16th—the day of admission. She left home feeling well and went to the house of this person, which was some distance from her home, and there a solution of soap and dettol (2 ounces) with 10 ounces of water was injected at 11 a.m. into the uterus by means of a Higginson syringe with an adapted nozzle adding 2½ inches to its length.

She collapsed immediately and thereafter complained of nagging mesial lower abdominal pain and vomited 3 times. She remained during the day in a more or less collapsed state at the house of the abortionist until 4 p.m., when she was taken home by car. On arrival she was noted to be collapsed.

From the onset of her symptoms till her admission to hospital at 8 p.m., that is during 9 hours, she had passed no urine although she had attempted to do so. There had been no vaginal blood loss.

Condition on admission. March 16th, 1946; 8 p.m. Shocked, restless, and slightly dyspnoeic; pale; temperature 97°F.; pulse 100; blood-pressure 90/75 mm. Hg. Tongue and lips dry.

The abdomen was tender and rigid, especially in its lower part, and a tender mesial swelling was found rising from the pelvis to within about 2 inches of the umbilicus. The catheter removed 3 ounces of urine which was brownish-red in colour. Basal sedimentation rate 8.

An intravenous glucose-saline drip was commenced and replaced by Rhesus negative Group O (IV) blood, 1 pint.

Operation. March 17th, 1946, 12.30 a.m. Laparotomy revealed a few ounces of dark sanguineous fluid in the peritoneal cavity. The uterus was enlarged to the size of an 18 week's pregnancy and had the "apoplectic" appearance found in concealed accidental haemorrhage. The surface was markedly congested and there were numerous scattered petechial haemorrhages on both anterior and posterior surfaces. There were 2 large areas of subperitoneal ecchymoses on the posterior surface, the one near the fundus and the other low down on the right side. The "apoplectic" condition was more emphasized on the right than on the left aspect of the uterus. The right Fallopian tube and ovary were congested, purplish black,

and were regarded as non-viable. The left Fallopian tube and ovary were slightly congested. The extravasation of blood extended along the right broad ligament to the wall of the pelvis on the right side and involved the utero-vesical pouch and the wall of the bladder. Subtotal hysterectomy and removal of the right Fallopian tube and ovary were carried out. It is important to note that the history indicated that these changes in the pelvic organs had evolved during a maximum period of about 13½ hours.

Uterus, Fallopian Tube and Ovary.

Bulky uterus (subtotal hysterectomy) and right Fallopian tube and ovary. The uterus is 15 cm. long, 14 cm. in its anterior posterior diameter and 11 cm. wide. The surface is congested, shows scattered petechial haemorrhages on both surfaces and 2 large subperitoneal ecchymoses on the posterior surface, one near the fundus and one lower down on the right-hand side. The Fallopian tube and ovary (4 × 3.5 × 2.5 cm.) are also grossly congested (Plate I). A sagittal section through

TABLE I.

Date	Serum			Intake	Urine		
	. Urea Mgm./100	Chlorides Mgm./100	Potassium Mgm./100	Ml./hour	Output Ml./hour	. Urea Mgm./100	Albumen Mgm./100
March 17th	115	—	—	78.0	2.1	193.0	650
,, 18th	119	540	23.6	62.7	0.74	—	, —
,, 19th	149	—	—	29.6	1.0	—	. 325
,, 20th	210	—	—	58.0	1.37	229.5	438
,, 21st	290	473	37.0	59.2	1.0	280.0	425

The patient was restored with a further pint of Group O (IV) Rhesus positive blood and 2 pints of plasma. By 6.30 a.m. on March 17th, the blood-pressure was 100/70 mm. Hg. Prophylactically a course of penicillin, 20,000 Oxford units 3 hourly, was commenced. The patient's blood was Group O (IV), Rhesus positive.

At 10.15 a.m. on March 17th 1½ ounces of blood-stained urine were obtained by catheter. In view of the oliguric state an intravenous drip of isotonic sodium sulphate solution (1 pint) was given and alkalies by the mouth. The general condition of the patient remained moderately good for several days but the oliguria persisted and altogether from the time of the injection of the dettol and soap to the time of death (5¾ days) only 8¼ ounces of urine were excreted. At no time was there oedema.

The data in regard to urine excretion, blood-pressure and the biochemical findings are represented in the accompanying tables (Table 1 and Fig. 1).

The pathological report by Dr. I. Doniach is as follows:

the uterus reveals the following state: There is a generalized congestion of the uterine wall whose veins are distended. The placenta lies closely applied to the anterior wall from the internal os up to the fundus. The sac contains a male foetus. The sac is separated from the posterior wall by peculiar gelatinous material most plentiful near the fundus where it extends to the edge of the placenta. The neighbouring 3 to 4 cm. of fundal portion of placenta is markedly haemorrhagic and friable, but the placenta beyond (attached to anterior uterine wall) appears normal. The fundal portion of uterine wall in direct relation to the junction of haemorrhagic placenta and gelatinous material is soft, pale and extremely friable. The upper posterior uterine wall is swollen, firm and intensely haemorrhagic for a length of 5 cm. —a classical appearance of infarction. The inner lining of the lower part of posterior uterine wall is firm, white and granular. Section of the ovary reveals a large corpus luteum and widespread haemorrhage. The foetus is well developed and preserved. It weighs 110 grams with the cord, sitting height 11.75 cm., crown to heel length 18.25
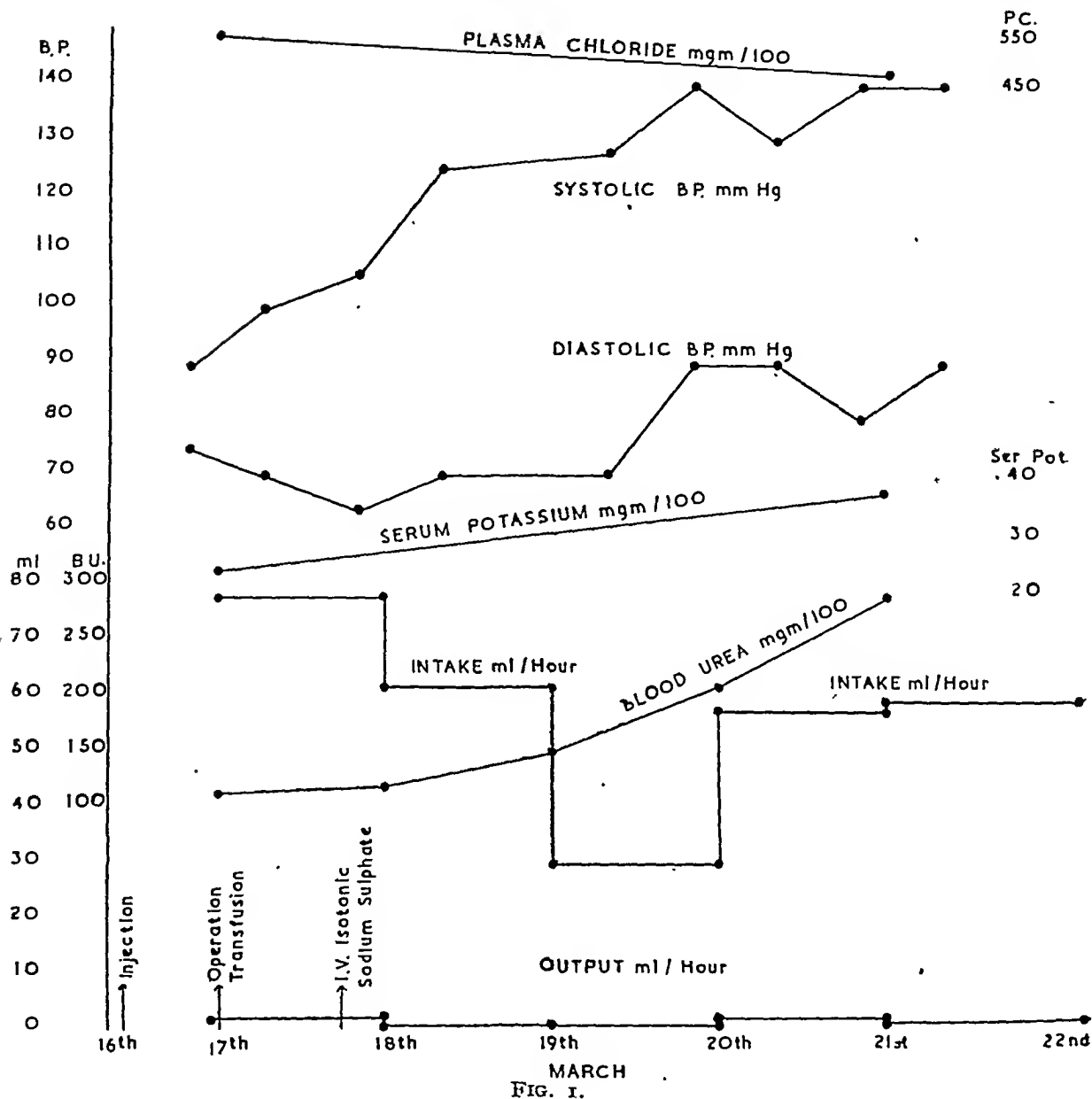
Fig. I.

cm. These measurements fit almost exactly Streeter's figures of 11.6 cm. sitting height and 108 grams for the average foetus at the end of the fourth lunar month of pregnancy. Professor Plimmer found plentiful fatty acids on analysis of of the gelatinous material and detected an aromatic smell which was not unlike that of dettol. Sections through the fundus show a thin outer rim of surviving uterine muscle fibres traversed by engorged veins; the underlying portion of muscle coat is replaced by an eosinophilic lake of hyaline material richly infiltrated with fatty acid crystals. It may well consist of altered muscle fibres and haemolysed red cells. The veins and arteries traversing this tissue show complete occlusion by granular debris; the arteries being more severely affected than the veins. Interior to the hyaline material lies amorphous fibrillary necrosed decidua. Section through the anterior wall near the fundus shows a similar change in the muscle and in

addition necrotic placenta lining its upper half, living placenta lower down, the demarcation being quite sharp. Similarly there is a sharp demarcation between necrosed and healthy uterine wall. Section of the upper portion of posterior wall shows a large area of necrosed myometrium demarcated from healthy muscle by a layer of polymorphonuclear leucocytes. In the necrotic wall there are partially thrombosed veins lying next to completely occluded arteries. Lower down, the vessels appear quite healthy. This section also shows a clear-cut demarcation between healthy and necrotic decidua parietalis. The picture suggests a local necrosis in the fundus region produced by the inoculum whose fatty acids are well seen in the necrotic tissue and in a few places inside clefts which are probably distended veins. The local arterial occlusion has also probably resulted from direct action of the inoculum. Section of the ovary shows enormous dilation of veins and capillaries and a widespread interstitial haemorrhage of fresh red cells. There are no fatty acid crystals present in the ovary. The haemorrhage can be seen in the corpus luteum and even in the sub-peritoneal collections of decidua cells. The picture in the ovary is one of haemorrhagic congestion such as is seen in torsion of the pedicle.

Kidneys.

The kidneys together weighed 490 grams. Sections show a well-marked separation of the tubules by interstitial oedema. Many glomeruli are funnel-shaped and contain eosinophil debris in their capsular spaces. Many proximal convoluted tubules show cloudy swelling and contain pink circular granular bodies which resemble degenerate cells. Many of the loops of Henle contain pigmented debris (cast material), the wide ascending loops show a regenerated lining epithelium and a lumen plugged by pigmented debris which is covered with a layer of flattened cells. The boundary zone shows numerous interstitial collections of lymphocytes and a few polymorphs gathered round cast containing tubules; and engorged vasae rectae. Many second convoluted tubules show changes similar to that seen in the ascending loops. Only one example was seen of cast material being extruded from a tubule. Benzidine staining shows the pigmented cast material to give a positive reaction for haemo-

globin. This is the classical picture of a " transfusion " or " crushing injury " kidney (Fig. 2). The pituitary showed a focus of necrosis in the pars anterior (a few days old). The liver showed centrilobular cell vacuolation.

It is not easy to account adequately for these remarkable changes in uterus and Fallopian tube and ovary. It is likely that the inoculum of soap and dettol introduced under pressure was forced into the large venous channels of the uterus, especially after it had reached and separated the edge of the placenta. It is possible that much of the necrosis was due to the direct action of the inoculum. The extensive haemorrhage into the musculature of the uterus and into areas where it is difficult to conceive that the inoculum could pass, for example, the ovary, may possibly be accounted for by the sudden thrombotic blockage of the main vascular channels, especially of the ovarian system. The marked development of the vessels, with a massive concentration of blood towards the placental area, which occurs during pregnancy, makes it not unlikely that serious and acute interference with one main part of the vascular return may produce rapidly occurring haemorrhage throughout the uterus and the adjacent structures.

However caused it is clear that the uterine changes here produced by an external agency closely simulate those seen in the " utero-placental apoplexy " of concealed accidental haemorrhage. This we know is produced as the result of those factors which commonly operate in diseased states to produce spontaneous abortion (Young, 1942). These factors are not well understood: they may arise from hormonal, nutritional or other causes.

The resemblance between the primary uteroplacental lesion found in this case and that occurring in concealed accidental haemorrhage extends to the renal lesion.

We have elsewhere described the characters of this lesion as found in 3 out of 4 fatal cases of concealed accidental haemorrhage (Young, 1942) and Bratton has reported similar findings (Bratton, 1941; and Young, 1942), (Fig. 3). This lesion is similar to that described by Bywaters and Dible (1942) in the syndrome following crushing injuries and consists of relatively minor changes in the glomerular and first tubular systems and of marked degeneration of the second convoluted and collecting tubules in which blood pigment casts of a granular or crystalline nature are present often in considerable quantity. The other

the identity of the essential clinical and pathological phenomena (Table II). There is tissue damage followed quickly by shock, anuria or oliguria, rapidly developing depreciation of tubular function with azotaemia, haemoglobinaemia and haemoglobinuria and, in severe cases, death from the fifth to the tenth day.

It is known that in concealed accidental haemorrhage the kidney lesion may, in rare instances, exhibit the picture of bilateral cortical necrosis. It is possible that the investigations of Trueta, Daniel, Barclay, Franklin and Pritchard (1946) on the renal circulation may have an important bearing

TABLE II.
Essential Similarity of Different Anuric States.

	Tissue damage	Shock	Anuria or Oliguria	Azotaemia	Kidney lesion	
					Tubular degeneration	Blood pigment casts
Crush syndrome	Muscle, etc	+	+	+	+	+
Mismatched transfusion	Blood	±	+	+	+	+
Extensive burns	Surface tissues	+	+	+	+	+
Obstetrical trauma	Uterus and pelvic tissues	+	+	+	+	+
Concealed accidental haemorrhage	Placenta, blood, uterus	+	+	+	+	+
Eclampsia	Placenta, blood	±	+	±	±	±

conditions in which this lesion is characteristically found are extensive burns and mismatched blood transfusion and it has been described after obstetrical crushing injuries (Young and McMichael, 1941). The lesion, in other words, is characteristic of a fairly wide generic group typified by massive tissue damage and it has a special interest for us in view of the increasing tendency to regard it as deriving, in those members of the group which have been intensively studied, from toxic materials produced at the site of the tissue damage.

That there exists a genetic similarity between these varied states is suggested by

on this question. These workers claim to show that under certain conditions, including toxic states, and as the result of an ischaemic process of neurovascular origin, the circulation in the renal cortex can be arrested whilst the total renal blood flow is shortcircuited through the medullary vessels. Such a process might explain not only the anuria and oliguria which constitutes such an important clinical feature of all our cases but also, in the case of persisting ischaemia, of the irreversible changes which culminate in bilateral cortical necrosis.

The study of the experimental animal
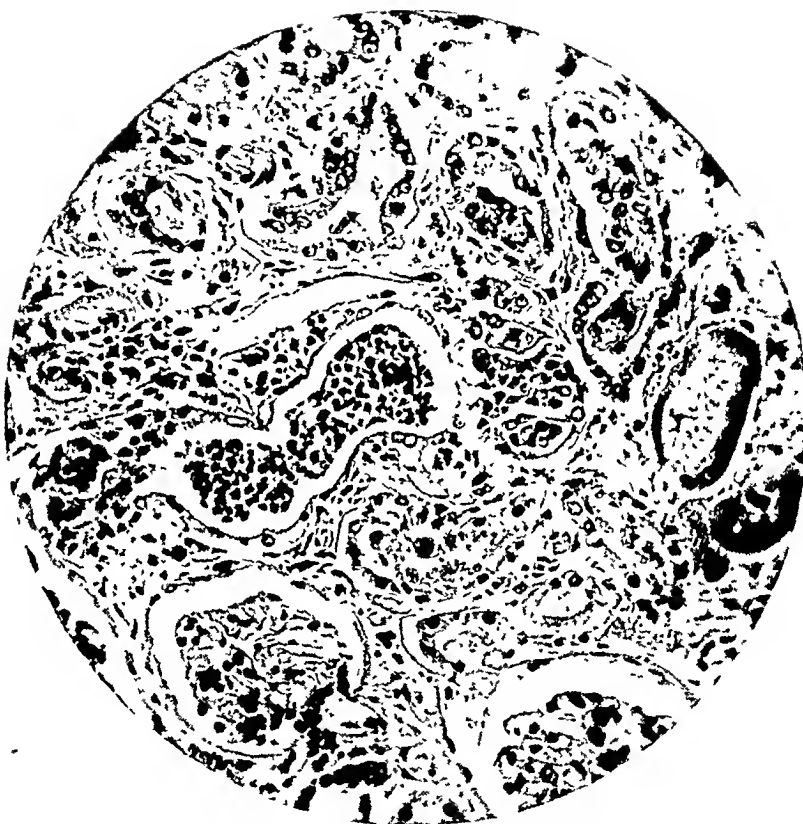
FIG. 2.

Criminal abortion. Anuria, uraemia and death on 5th day. Kidney showing degeneration of the second convoluted tubules with desquamation of epithelium and blood pigment.   × 205

J.Y.

FIG. 3.

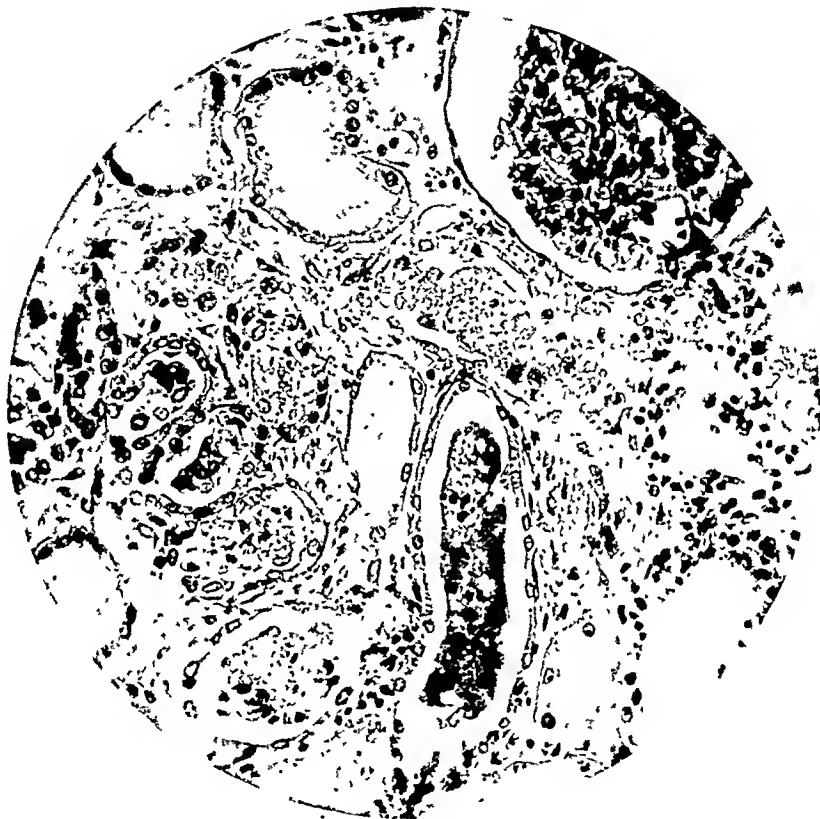Concealed accidental haemorrhage. Anuria, uraemia and death on 6th day. Kidney showing degeneration of second convoluted tubules, desquamated epithelium and albuminous and blood pigment casts.

J.Y.

× 205

PLATE I.
Criminal abortion. Showing " apoplectic " condition of the uterus.

has thrown some light on the manner in which the products of tissue damage operate (Eggleton, Richardson, Schild and Winton, 1942; Eggleton, 1944; Corcoran and Page, 1945). This experimental work has consisted in the main in the reproduction of the crush syndrome. The limb of the anaesthetized animal is obstructed for a sufficient time (4 or 5 hours) by a tourniquet. The muscles may be crushed at the same time. Liberation of the tourniquet allows the products of tissue disintegration to escape into the general circulation. This is followed almost immediately by anuria or oliguria and a marked depreciation in urea and creatinine clearance. This lowering of renal function is not due to the "shock" process, which is an invariable accompaniment of the experiment, for it is present when measures are taken to counteract the fall in blood-pressure and to restore the blood volume. The evidence seems to indicate clearly that, whilst the "shock" (with low blood-pressure, massive loss of plasma to the damaged limb and haemoconcentration) may, in the ordinary experiment, partly explain the initial anuria or oliguria on the basis of lowered glomerular pressure, the main and all the irreversible changes are determined by materials escaping from the damaged tissues. The exact nature and mode of production of these substances is not known. There is evidence that the anuria is due to renal ischaemia with, perhaps, as contributing factors tubular blockage from blood casts and debris. In the opinion of most observers it is necessary to postulate also a direct toxic action on the tubules (haematin, breakdown products of tissue protein).

Intravascular Haemolysis.

The part played by intravascular haemolysis in the causation of the renal lesion has been variously interpreted. Common to all the anuric states it seems to be the sole factor in mismatched transfusion. For this reason the question naturally arises as to how far it may be of primary importance. To this the available evidence does not provide a clear answer. Simple blockage of the tubules by the blood pigment is not a sufficient explanation of the anuria for this is present when the blood casts are at a minimum. Even in the case of mismatched transfusion it would seem that a nephrotoxic action must be postulated for in man haemoglobin itself liberated into the blood stream as in proxysmal haemoglobinuria or by injection does not produce anuria.

There is no evidence to incriminate the blood transfusion given in the case under discussion. It is clear that the kidneys were gravely embarrassed before the first blood was administered. During the 9 hours following the injection of the dettol-soap mixture only 3 ounces of urine were excreted and we may assume that this took place during the earliest phase.

Pre-eclampsia and Eclampsia.

Whilst the pronounced renal lesion distinguishes the toxaemia of concealed accidental haemorrhage from that typical of the eclamptic state, there is evidence that these two states may have a common genetic background. This is exemplified in the frequency with which they occur in combination. It is common knowledge that a pre-eclampsia may terminate in concealed haemorrhage and that in eclampsia the placenta after delivery may exhibit a large retroplacental haematoma. Moreover the long recognized association of intravascular haemolysis and haemoglobinuria with eclampsia, and the frequent pigment deposits in the tubules of the eclamptic kidney serve to forge further links between

E

eclampsia and those toxic states which are due to the liberation into the circulation of the products of tissue damage. Since Schmorl (1893) described yellow pigment in the collecting tubules of the eclamptic kidney a number of authors on the Continent and in this country have described similar appearances, sometimes with tubular degeneration and necrosis (Brütt and Schumm, 1918; Fahr, 1924; Seitz, 1927; Dunn and Baird, 1933; Spitzer, 1934; Bratton, 1941; Young, 1942). At the same time these appearances are neither so prominent nor so frequent in eclampsia as in the other states referred to. The total phenomena are in keeping with the view that whilst there runs throughout the varying phenomena a common genetic thread the modes of expression differ with the differences in the basic lesion.

In eclampsia, as we have shown in previous communications, there is a massive placental lesion involving from one third to one half of the organ. This is easily recognisable in those cases where there is time for its evolution into visible form, that is where the eclamptic seizure is followed by the intrauterine survival of the foetus. On the other hand where, as is usual, foetal death or delivery occurs within a short interval, there may be no conclusive naked eye or even histological evidence of this ischaemic lesion. These observations we have regarded as in keeping with the conception of a placental poison produced during the earlier stages of the disintegration of the damaged organ (Young, 1914, 1942). The discovery that in the ischaemic limb of the experimental animal the toxic materials are produced within a few hours lends support by analogy to such a conception. It finds further evidence in its favour in the conditions obtaining in the human experiment which forms the subject of this communication.

We are indebted to Miss J. Dewe, artist to the British Postgraduate Medical School, for the preparation of the coloured plate, and to Mr. E. V. Willmott, A.R.P.S., head of the Department of Photography in the British Postgraduate Medical School, for the microphotographs.

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Combined Anterior Pituitary Necrosis and Symmetrical Cortical Necrosis of the Kidneys following Accidental Haemorrhage

BY

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DETAILS of a case of necrosis of the anterior pituitary and symmetrical cortical necrosis of the kidneys and of cases of cortical necrosis are submitted because of the rarity of both these conditions and therefore of the need to report such information as becomes available.

CASE I. 3859/43, K. J.

An unmarried girl, aged 15 years 10 months, a primigravida with an uneventful previous medical history. First day of last menstrual period, February 1943, first week. Expected date of confinement, November 1943, second week.

Although she knew herself to be pregnant she had not made preparations for her confinement or had any ante-natal supervision. She is said to have been quite well until September 16th, 1943, when she had a fall. This not very serious accident was followed, within an hour, by vaginal bleeding which continued intermittently for another hour. Bleeding then ceased but began again later in the evening, accompanied by pains in the " pit of the stomach ". These pains became rhythmical in character, occurring at intervals of 5 minutes, and she now thought she " might be aborting ". She therefore came to hospital in the early hours of the morning of September 17th.

When seen at 3 a.m. her condition was poor, her colour was bad with the pallor of shock or possibly blood loss and she was obviously anxious. Oedema of the legs was present to the level of the knees and the face was markedly puffy. She was well developed and well nourished.

Cardio-vascular system. Heart not enlarged, pulse poor in volume, rate 110. Blood-pressure 110/65.

Abdomen. Enlarged to the size of a 36 weeks' pregnancy, the uterus palpable as a hard, tense tumour. Foetal parts could not be identified nor was the foetal heart heard. On rectal examination the cervix could be identified one finger dilated, with the vertex presenting.

Uterine contractions were occurring at intervals of 10 minutes. There was slight continuous bleeding *per vaginam*. A provisional diagnosis of toxaemia of pregnancy with accidental haemorrhage was made.

Treatment and progress. As the accidental haemorrhage had now become revealed it was hoped that there would be spontaneous delivery as uterine contractions were occurring regularly.

At 9.30 a.m. there had been little change in her condition, but uterine contractions were beginning to decrease in intensity and frequency. The uterus had not appreciably increased in size and although still tense could not be described as " woody ". Labour ceased for some hours during the afternoon, but pains returned with markedly increased severity at 5 p.m. At 6 p.m. her pulse was 136 and her blood-pressure had fallen to 98/76. The cervix was now fully dilated and the small foetal head well down in the pelvis. At 7.30 p.m. she was delivered spontaneously of a macerated female foetus weighing 4 pounds 7 ounces, and measuring 19 inches in length. The placenta and membranes were expelled at 8 p.m. There was no excessive loss during delivery, but about 10 ounces of blood and clots were expelled with the placenta, which showed numerous infarcts. Blood clot was adherent to the maternal surface of the placenta. Labour had lasted approximately 24 hours.

Subsequent progress. Following delivery her condition showed some improvement and she took

fluids well and slept during the rest of the night without drugs. During the 24 hours she passed 900 ml. of urine.

On September 18th she complained of drowsiness, and during that 24 hours passed only 90 ml. of urine, although she still took adequate fluids by mouth. The subsequent fluid intake and output are indicated in the accompanying chart, Fig. 1, and show the sudden and pronounced oliguria. The haemoglobin on September 20th was only 22 per cent and the blood urea 184 mgm./100 on the following day.

From the 21st, there began a rapid deterioration in her condition, the blood urea had risen to 216 mgm./100 on September 24th, and she died the following day.

Throughout her illness and in spite of the very high blood-urea estimations, her mental condition remained clear. She was drowsy but could be roused sufficiently to carry on intelligent conversation.

Treatment had consisted of the administration of adequate fluids, particularly glucose, which she took well. The oedema of the legs present at the
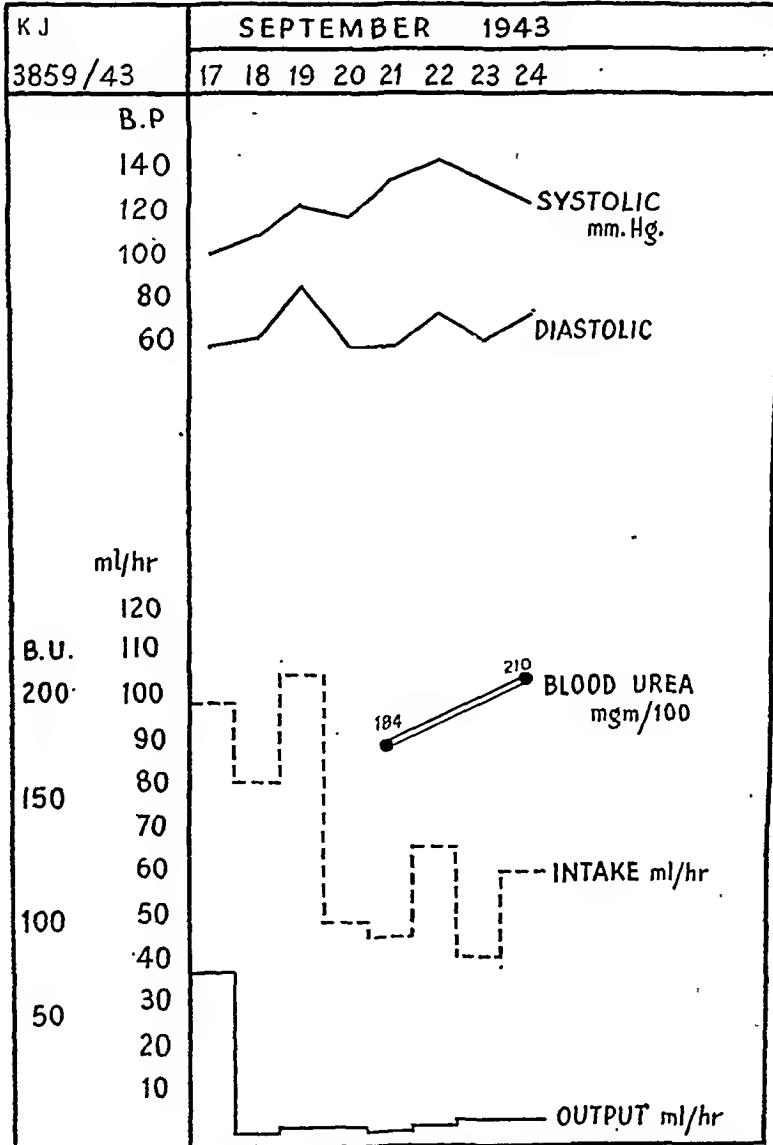
FIG. 1.

time of admission gradually disappeared, but the puffiness of the face persisted. This was the only obvious sign of fluid retention.

Postmortem examination was carried out on September 26th, and the following conditions were observed.

Kidneys. Both kidneys were enlarged and the cortex, apart from a narrow subcortical area of normal tissue, was entirely necrotic and structureless, the appearance typical of symmetrical cortical necrosis.

Liver. Not grossly abnormal.

Thyroid. Enlarged, but not abnormal.

Pituitary gland. Necrosis of anterior lobe.

Microscopical examination of sections of the kidneys showed typical and extensive cortical necrosis.

DISCUSSION.

In considering this case, which was observed some 2 years before that described so completely by Doniach and Walker, the many points of similarity between the cases are at once apparent, and are shown in tabulated form in Table I.

Two similar cases are described by Hügin (1946).

The first is that of a 5-para, aged 35 years, in whose obstetric history was known evidence of toxaemia—oedema of legs in a pregnancy 11 years previously, followed by "kidney disease" in the puerperium, and hypertension (blood-

TABLE I.

	Doniach and Walker	Grasby
Duration of pregnancy	28–30 weeks	28–30 weeks
Blood-pressure:		
Maximum	155/95	150/80
Minimum	130/80	110/65
Albuminuria/1000 ...	7.5	8
Oedema	Legs and face (slight)	Face, legs and lower abdomen (slight)
Shock	Severe	Severe
Haemoglobin gm. per cent	5	3
Blood urea, mgm./100	106–216	182–216
Lactational changes	nil	nil
Death-day of illness	7th	7th

The pituitary gland showed "complete necrosis of the anterior lobe cells, with the exception of a small area anteriorly". The sections were examined by Professor Payling Wright, who commented that this form of necrosis was not uncommon in conditions of haemorrhage but not, as far as was known, previously reported in association with cortical necrosis. The extent of the necrosis is shown in Fig. 2, and is identical in type and appearance with that reported by Doniach and Walker (1946).

pressure 160/90) in a pregnancy 2 years before that under review. In the pregnancy described, the patient is said to have been "well, and less tired than in previous pregnancies but some dyspnoea on exertion and occasional headaches and spots before the eyes, swollen ankles and itching of the hands, especially during the last weeks" are reported. Severe pain followed by vaginal bleeding occurred during the night

and on admission to hospital her condition was grave. Only a few ml. of pale urine were obtained by catheterization. Foetal heart sounds were not heard. Hysterotomy was performed and separation of a normally, situated placenta discovered. The placenta showed numerous infarcts. There was complete anuria after· operation, in spite of bilateral renal decapsultation, and death occurred 7 days later with a mounting blood urea. Postmortem examination revealed the typical changes of symmetrical cortical necrosis, necrosis of the anterior pituitary cells, the gland showing an apparent attempt at new formation of capillaries and thrombosed vessels, but without changes in the vascular wall which were found in other organs, notably the kidneys. The liver showed the changes of eclampsia, while the breasts showed lactational changes.

The second case is that of a primigravida aged 29 years, with no previous history of severe illness or abortions. Two antenatal examinations revealed no abnormalities. Severe epigastric pains occurred without warning and were followed by the cessation of foetal movements, the onset of abdominal pains and regular contractions. The patient was unable to void any urine. Vaginal bleeding then followed, the pains diminished and she fell asleep, only to be interrupted by sudden eclamptic convulsions. A recently dead foetus was extracted with forceps, the placenta showing " extensive infarcts ". Decapsulation of the kidneys was performed for complete anuria and the patient died on the 15th day after delivery. Postmortem examination showed the typical changes of symmetrical cortical necrosis, necrosis of the cells of the anterior pituitary—" not a nucleus visible " —and eclamptic changes in the liver. The kidneys also showed " nephrosis and haemorrhagic nephritis, with extensive cast

formation and fatty degeneration ". The blood urea is given as 300 mgm./100.

Unfortunately the brief reports of these cases do not give the blood-pressure readings, haemoglobin or biochemical findings. The summary of the pathological findings is given as " eclamptic necrosis of the liver, softening of the brain substance, cortical necrosis of the kidneys, necrosis of the anterior pituitary and intrauterine death of the foetus. The changes were not so marked in the second case, i.e. the renal vessels were hardly changed, there were no thromboses, and although there was haemorrhagic necrosis of the anterior pituitary there were no proven changes in the walls of the vessels or thromboses ".

In these 4 cases—the first to be recorded —those described by Hügin show interesting variations, notably the previous history in each of his 2 cases of pregnancy toxaemia and the postmortem eclamptic changes, confirmed microscopically in the liver. No such changes were demonstrated in the case reported by Doniach and Walker nor in the case above described. A further interesting feature is the report by Hügin of apparent attempts at " reorganization " in the pituitary and, in the second case, an apparently less severe degree of necrosis, coincident with a longer period of survival after the onset of acute symptoms of retroplacental bleeding.

Variations in the severity and rapidity of onset of symptoms of pituitary insufficiency following postpartum haemorrhage are well recognized, from the slowly developing condition originally described by Simmonds (1914) to the mild types of pituitary emaciation described by von Bergmann (1934) and others. Sheehan (1938; 1939) who particularly investigated and described postpartum pituitary necrosis considered the thrombosis of the vessels due to the haemorrhage and collapse during delivery but that recovery was pos-

sible in the less severe cases. Recovery is in fact accelerated by the occurrence of a subsequent pregnancy. Sheehan and Murdoch (1938; 1939) have reported not only symptomatic improvement but, in a patient (Case 5) who was given intensive hormonal therapy (gonadotrophic and oestrogenic) to render pregnancy more probable and who did become pregnant, immediate and subsequently permanent improvement of the pituitary insufficiency. It is suggested that this improvement is due to the physiological hypertrophy of the remaining undamaged anterior pituitary cells occasioned by the subsequent pregnancy.

Such possible variations in the degree of pituitary necrosis may explain the less extensive disease and evidence of lactational changes in the cases described by Hügin. Similar variation in severity is recognized in symmetrical cortical necrosis, which, as Doniach and Walker point out in their detailed review is explicable by a relatively simple pathology—reflex vasoconstriction following severe haemorrhage in an already anaemic patient, leading to vascular degenerative changes and thrombosis—which can equally well be applied to explain the pituitary necrosis.

Details of 2 cases of cortical necrosis are reported to illustrate less severe degrees of the condition.

CASE 2. 4966/43 N.A.

Married, aged 40 years; 5-para; the last pregnancy terminated in miscarriage at the 28th week, no cause being known. She had not had antenatal supervision in any of her pregnancies, which had been normal, and there was no history of serious illness.

First day of last menstrual period not known, but was early in May 1943. Expected date of confinement early February 1944.

The patient stated that the pregnancy had appeared to be quite normal until December 3rd, 1943, the day before admission to hospital, when "she started losing". There was no pain with this haemorrhage, but she thought she may have lost almost 10 ounces of blood. She did not look upon this as particularly serious and did not call in her doctor until the following day. Information could not be obtained as to her previous condition or blood-pressure.

On admission to hospital on December 4th, 1943, the patient was well nourished; good build; mucous membranes very pale; general condition fair; no shock; oedema of legs as high as the knees.

Cardiovascular system. Heart normal in size, no bruits; blood-pressure 190/140.

Respiratory system. No abnormalities discovered.

Urine. Albumin, plus 3 (9/1000 in Esbach).

Abdominal examination. Immediately below the umbilicus was a small haematoma of the abdominal wall, 1½ by 1 inch in size, and apparently quite superficial. The patient believed it had appeared the previous day. The abdomen was enlarged to the size of a 36 weeks' pregnancy, the uterus on palpation being hard, tense and tender. There was no area of localized tenderness. Foetal parts could not be identified nor could any foetal heart be heard. Contractions of the uterus could not be felt and the patient did not appear to be in labour. On rectal examination the os could be felt undilated. There was a continuous slight haemorrhage from the vagina, which had continued since the first haemorrhage on the previous day. A diagnosis of toxaemia with accidental haemorrhage (mixed) was made.

Treatment. The membranes were ruptured and 15 ounces of clear liquor amnii were run off without difficulty and without discomfort to the patient. A course of injections of pitocin 2 units every half hour was also commenced and continued for 5 injections. Good uterine contractions ensued with no increase in the amount of blood loss from the vagina.

At 9.30 p.m. she was delivered spontaneously of a macerated male foetus weighing 2 pounds 9 ounces, and measuring 14 inches in length, corresponding with a 29 weeks pregnancy. There was no bleeding with the delivery of the foetus. The placenta and membranes were delivered intact half an hour later, and were accompanied by 12 ounces of dark blood and old blood clot. The uterus contracted well after delivery and the patient's

condition at the end of the third stage was quite satisfactory. Temperature 98°F., pulse 100; respiration 20.

The placenta was found to contain numerous small infarcts and much old blood clot adherent to the maternal surface. The retroplacental haematoma had not ruptured into the amniotic cavity.

Subsequent progress. The patient's condition on the following day, December 5th, was quite satisfactory. The blood-pressure was 160/100, there had been no bleeding during the night and she had passed urine on 2 occasions.

On December 6th, she appeared rather drowsy, her tongue was dry and coated, and she did not appear as well as was to be hoped. During the 24 hours she passed 450 ml. of urine only and this oliguria was particularly noted because she had taken fluids well. The blood urea was estimated and found to be 232 mgm./100.

The fluid intake and output and the blood urea estimations are recorded for convenience in a chart (Fig. 3), and show a progressive oliguria and rising blood urea, with fluid retention until December 16th, when there commenced a sudden polyuria. This markedly increased urinary output continued, with, however, a gradual fall in total fluids excreted until December 27th, when she again passed large quantities of dilute urine. She was by now unfortunately incontinent and exact measurement of the amounts was impossible. This second polyuria coincided with a remarkable fall in the blood urea.

The following are abstracts from the day to day records:—

7.12.1943. Intravenous dextrose 10 per cent, 550 ml.; intravenous dextrose 25 per cent, 10 ml.

8.12.1943. Drowsy, but quite rational and taking fluid well. Oedema, plus 3; fluid output, 230 ml.; blood-pressure, 210/130; haemoglobin, 35 per cent; intravenous dextrose, 50 per cent, 60 ml.

11.12.1943. Some improvement in general condition, patient talking and quite rational. Taking fluids well but fluid output less than 300 ml. for 3 days. She passed no urine during the last 24 hours. No oedema. Blood urea 312 mgm.5/100; blood-pressure, 200/120.

13.12.1943. Condition not so good. There has been a return of the odema, and although she is completely rational she is obviously uraemic, with

gasping respiration, lack of interest in her surroundings, and severe skin irritation. Blood-pressure, 196/130; blood urea, 496 mgm./100; urine urea, 1,480 mgm./100; standard urea clearance 3.9 per cent average normal.

15.12.1943. Blood urea 408 mgm./100; .condition much worse.

16.12.1943. Sudden polyuria; output 1,700 ml. in 24 hours; blood-pressure, 130/90; outlook seems more hopeful.

17.12.1943. Still maintaining a good fluid balance, but there is no improvement in her condition. No oedema.

20.12.1943. She is still drowsy, disinterested, pale and now beginning to look cachetic. The skin irritation persists. Intake and output approximately equal at 1,400 ml.; blood-pressure has risen from 140/95 to 170/105.

21.12.1943. Blood urea, 932 mgm./100; urine urea 1,720 mgm./100; urea clearance 3.2 per cent average normal.

22.12.1943 to 2.1.1944. Gradual deterioration in patient's condition. Still passing from 1,000 to 1,500 ml. dilute urine, specific gravity c. 1008, and taking fluids quite well. Her mental condition is getting confused and although she recognizes people around her she is roused only with an effort. Towards the end she became incontinent, but the polyuria was even more marked.

On December 26th she passed 400 ml. urine which contained one third part by volume of pure pus. Until then the urine had contained no pus cells but occasionally a trace of albumin. Cause for this pus was not discovered.

On December 29th the blood urea was 464 mgm./100; but there was no improvement in her condition and she died on January 2nd, 1944.

Treatment during this period was purely symptomatic.

Microscopical examinations of the urine during the course of the illness revealed red blood corpuscles and granular casts on 2 occasions only, namely the second and third days of oliguria.

A postmortem examination was made and revealed the typical kidney damage associated with symmetrical cortical necrosis confirmed by microscopical examination. Other organs were not grossly abnormal and there was little evidence of toxaemia of pregnancy. The uterus was not infected.

In reporting on the sections Dr. de Nevasquez
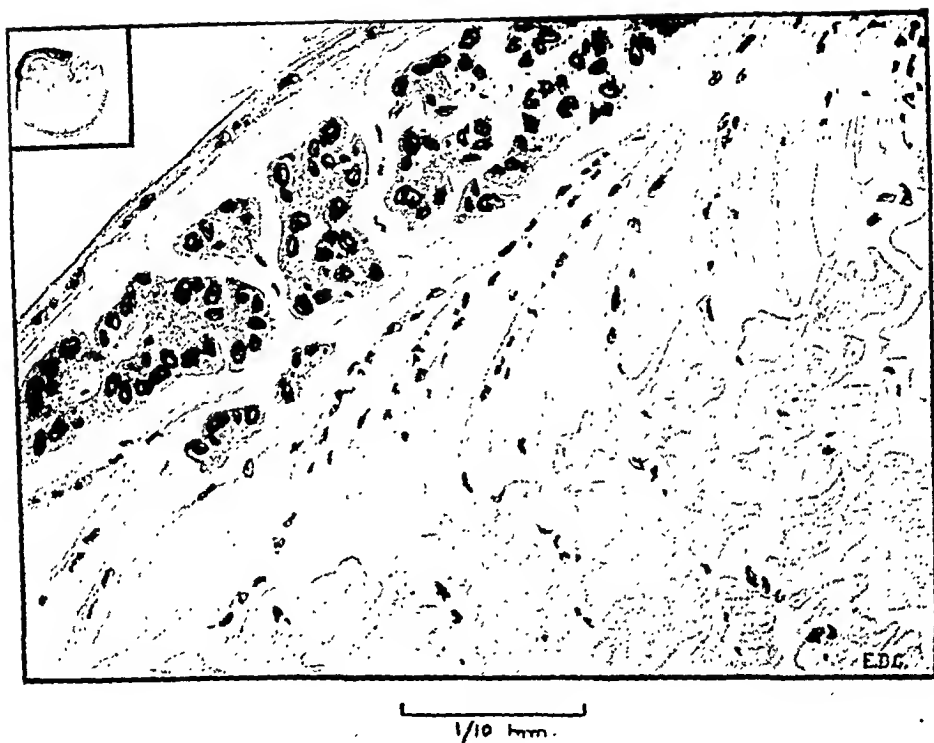
FIG. 2.

Necrosis of anterior pituitary gland, the few remaining undamaged cells are shown to the left, the necrotic tissue to the right. *Inset*: Drawing to show the exceedingly small fringe of remaining healthy tissue in the pituitary gland (shaded dark in the upper left quadrant).

E.D.Y.G.

noted that although the kidneys showed typical cortical necrosis the extent of the lesion was rather less than that usually seen.

Other features of particular interest in this case were the evidence of arterial spasm to which

CASE 3. 2506/45, R. P.

This patient was a 2-para and did not give any history of illness or abnormality in either of her previous pregnancies. Her previous medical history was equally uneventful.
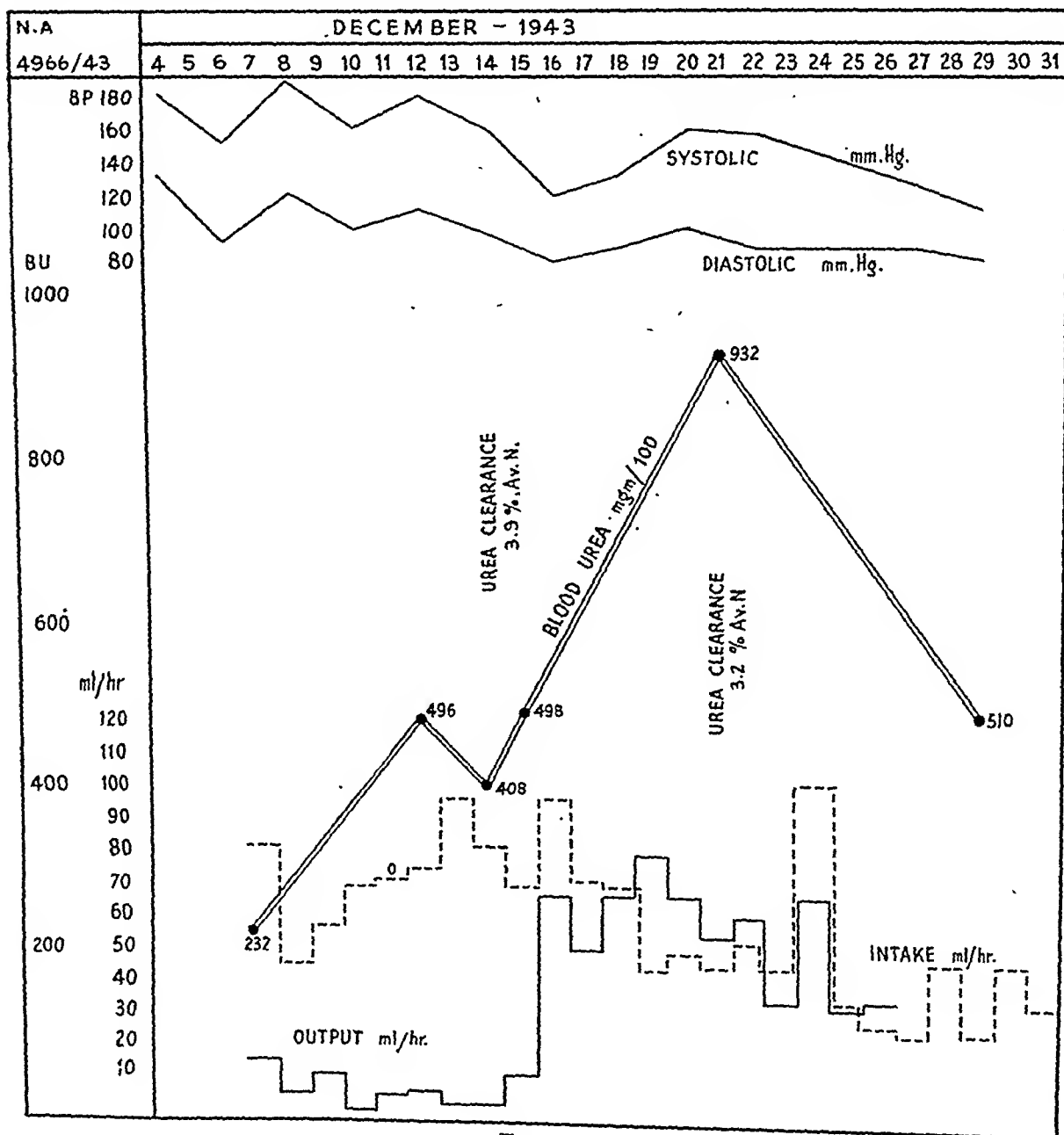
FIG. 3.

Doniach and Walker specifically draw attention, the severe anaemia and the unusually high blood urea.

First day of last menstrual period was early in March 1945. Expected date of confinement about second week December 1945.

She had had no antenatal supervision but stated she had been well until October 5th, 1945, when she had an attack of vomiting associated with epigastric pain. The pain became worse and she was seen by her doctor on October 7th when the

was admitted to hospital with a tentative diagnosis of accidental haemorrhage and toxaemia.

On admission to hospital on October 7th, 1945, her condition was very shocked and pale. Pulse poor in volume; rate below 105. Generalized
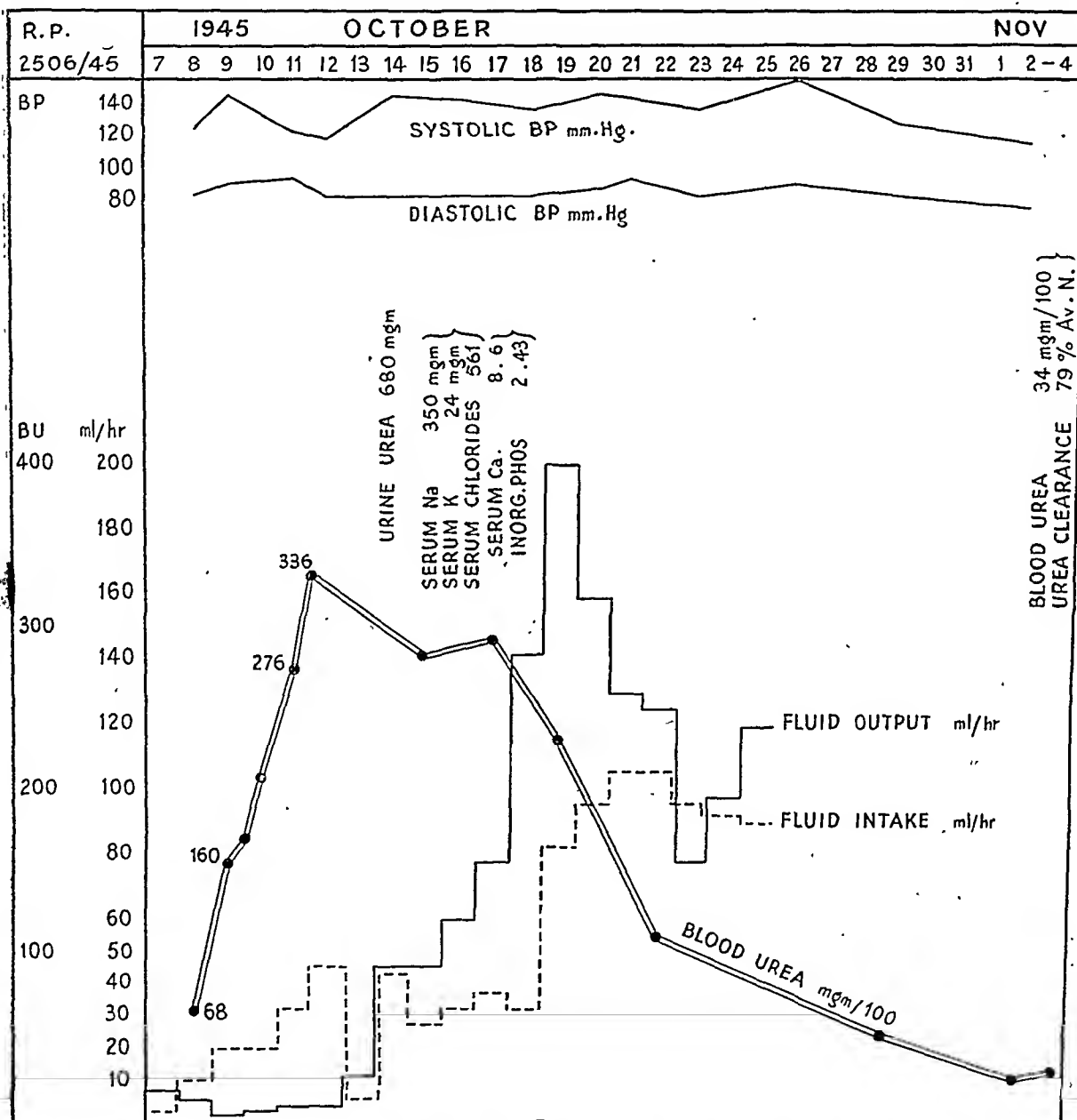
FIG. 4.

pain was severe in the abdomen and back. Her blood-pressure was then found to be 160/110 and the urine found to contain a trace of albumin. She

oedema; blood-pressure, 110/90; urine contained albumin, heavy cloud. The uterus was enlarged to correspond with a 32 weeks' pregnancy. It was

tense and hard, and tender. Foetal parts could not be palpated nor could the foetal heart be heard. There was a slight loss *per vaginam*.

In the belief that there had been a considerable intrauterine haemorrhage a blood transfusion of cross-matched blood was given, and later in the evening the membranes were ruptured.

On the following morning she expelled a macerated male foetus of about 28 weeks' duration. The placenta and membranes were expelled complete and without further haemorrhage, the placenta showing multiple infarcts and some old blood clot adherent to the maternal surface. The uterus contracted well and her general condition was much more satisfactory. The blood-pressure was 130/90. She had not passed urine since admission and at 10·30 p.m. she was catheterized and 70 ml. of urine withdrawn. There was no blood in the urine. It was decided, because of the oliguria, to give 370 ml. of 50 per cent glucose solution intravenously. On October 9th catheterization yielded 15 ml. of urine containing albumin but no blood. The oedema persisted and there was now papilloedema of the fundi, more marked in the right disc. She was given 50 ml. of 50 per cent glucose intravenously followed by 1,100 ml. of 3·4 per cent sodii sulph. solution.

On October 10th there was, perhaps, slight improvement although she was drowsy and the oedema remained unchanged. Catheterization yielded 25 ml. of urine containing no obvious blood and only occasional red blood corpuscles on microscopical examination. The oliguria continued with gradual deterioration in her condition until October 14th, when she passed 1,100 ml. urine of low specific gravity (1005–1006). The diuresis continued and there was an immediate and dramatic improvement with increased mental acuity, improved vision and lessening of the oedema, and this improvement was maintained. She finally made a complete recovery and was discharged from hospital on November 8th. When seen 3 weeks later her condition was quite satisfactory, her blood-pressure was 120/80, there was no albuminuria and her urea clearance was 79 per cent average normal. The day to day record of fluid intake and output, and clinical and biochemical findings are recorded in the chart (Fig. 4).

The diagnosis in this case was considered to be symmetrical cortical necrosis following toxaemic accidental haemorrhage, although, as in so many reputed recoveries from this condition, the diagnosis rests only on the similarity between these cases and known cases proved at autopsy. Dexter and Weiss (1943) comment that the evidence for the diagnosis in the majority of reported recoveries is very inadequate but although biopsy of the kidneys, to put the question of diagnosis beyond doubt, was not performed in any of their cases, apparently genuine cases of recovery have been reported by Gibberd (1936), Dingle (1943) and more recently by O'Sullivan and Spitzer (1946) who also give a complete bibliography.

The 3 cases here described would, therefore, appear to represent variations in severity of the same clinical and pathological syndrome, the first culminating in combined cortical necrosis and pituitary necrosis, the second presenting the classical features of symmetrical cortical necrosis with, however, clinical evidence that recovery might have occurred and pathological evidence of less renal destruction than is commonly seen, while the third case probably demonstrates a recovery.

SUMMARY.

1. A case of combined anterior pituitary necrosis and symmetrical cortical necrosis of the kidneys following concealed accidental haemorrhage is described.

2. A case of symmetrical cortical necrosis of the kidneys with clinical evidence of a less severe form of the syndrome is described, with confirmatory pathological evidence.

3. A probable recovery from established symmetrical cortical necrosis of the kidneys is reported.

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An Unusual Case of Adherent Placenta Treated in an Unorthodox Manner[*]

BY

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In June 1932 Mrs. S. came under my care when 32 to 34 weeks pregnant, with toxaemia which had persisted for many weeks.

Two unsuccessful attempts were made to induce labour by mechanical means; bleeding did not occur. The foetal heart was no longer audible when the second attempt at induction was made 6 weeks after the expected date of delivery. Four weeks later, as labour had still not begun, it was decided to empty the uterus operatively. The cervix was dilated as the first step in a vaginal hysterotomy, and it was then found that the placenta was praevia, so the attempt at vaginal delivery was abandoned. There was very little bleeding. The patient was transferred to the theatre and the abdomen opened. The uterus presented a curious greyish-brown appearance and seemed almost avascular. It was incised as in the classical operation and its wall proved to be only a few millimetres thick. A large amount of odourless liquor escaped and the foetus was extracted. The uterus then collapsed like a bag. There was absolutely no uterine muscle tone, but in spite of this a complete absence of bleeding. There was a central placenta praevia. It was reduced to a thin, mummified, parchment-like structure densely adherent to the uterine wall and no plane of separation could be found. A few fragments of placenta were removed, the cord was cut off short and the uterus was marsupialized by stitching the edges of the uterine incision to the rectus sheath. The uterine cavity was packed with gauze soaked in acriflavine. She had a febrile convalescence. No lochia appeared and no material recognizable as placenta was passed through the abdominal wound or from the vagina. She was discharged from hospital ten weeks later with the superficial part of the abdominal wound not then healed.

Three months later Mrs. S. wrote that she was living a completely normal life. The wound was healed and as she had had 3 quite normal and painless menses she wanted to know what she should do about another pregnancy.

In 1934, that is about 2 years later, she conceived again and had a completely uneventful pregnancy.

She went into labour at the 35th week with the child presenting by the breech and I immediately undertook a Caesarean section again. There was one very thick adhesion from the old scar in the uterus to the abdominal wall. This was not divided and the uterus was incised alongside it. The wall was extremely thin. As soon as it was touched with the knife liquor amnii gushed out. A female child weighing 5 pounds 3 ounces was delivered and cried

well. An attempt was then made to trim and repair the uterus but so much bleeding occurred that this was abandoned and the uterus closed as rapidly as possible. On this occasion convalescence was normal except for some trouble with the chest. The patient was discharged on the 24th day with her abdominal wall healed. The child was healthy, was entirely breast fed and 4 ounces above its birth weight.

Mrs. S. was seen again in October 1946. She remains very well. Menstruation is normal and painless. There is no sign of ventral hernia. The pelvic organs are normal and there is surprisingly little fixation of the uterus.

Avoidance of Catheterization following Vaginal Plastic Operations*

BY

ARTHUR A. GEMMELL, M.C., M.D., F.R.C.O.G.,

Lecturer in Obstetrics and Gynaecology, University of Liverpool.

SOME months ago I was discussing with my students the after-care of patients who had been operated upon for prolapse. Miss June Tyson drew my attention to a paragraph in Hamilton Bailey's 1944 edition of "Pye's Surgical Handicraft" reporting the reduction in the catheterization rate in the Mayo clinic from the instillation of one ounce of 0.5 per cent Mercurochrome into the bladder following pelvic operations.

I have found that it is patients who have had a vaginal plastic operation who have the greatest difficulty in establishing spontaneous micturition. The introduction of Carbachol has been of great assistance in all cases other than prolapse cases. I have always disliked the use of an indwelling catheter for these patients as in so many of them it seems to cause additional discomfort whilst repeated catheterization opens the way to infection.

We decided to try the use of 0.5 per cent Mercurochrome in cases of prolapse. This is only a preliminary report, as my house surgeon, Miss Quinn, has really conducted the investigation and will later report fully. For this purpose we record here the results in 63 cases in which Mercurochrome was used and, as a control, the 50 previous cases in which it was not used. Only cases for whom both an anterior and a posterior wall repair were undertaken are included in both series. The same ward sisters were in charge throughout both series except for a few cases in one ward towards the end of the series of treated women.

The figures are as follows:

	Without Mercurochrome	With Mercurochrome
Total cases	50	63
Patients catheterized ...	36	6
Percentage catheterized ...	72.0	9.5
Difference in percentage catheterized		62.5
Standard error of this difference		±9.15

Therefore the difference is 6.83 times its standard error.

.The statistical check has been worked out by Mr. W. J. Corlett of the University of Liverpool's Statistical Department and because the difference is so many times its standard error he concludes that it is " a difference with a negligible probability of having arisen by chance ".

No explanation has so far been given for the effect produced by Mercurochrome. My suggestion is that it acts as an irritant and that this irritant action has a greater effect upon the nervous control of the bladder than has the inhibitory action of the pain or tissue damage in the area of operation.

In support of this idea of irritant action it should be stated that we have on four occasions (twice during the investigation and twice since) seen the use of Mercurochrome followed by haematuria. All 4 patients settled down on irrigation of the bladder with normal saline without further incident and none of the 4 has had any further bladder disturbance when seen for a "follow-up" visit 3 months after operation.

Labour in an Iron Lung
(REPORT OF A CASE)

BY

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Obstetrical and Gynaecological Registrar,
Queen Elizabeth Hospital, Birmingham.

THIS case is reported on account of its rarity, and also to put on record the difficulties that were met with in dealing with it.

Mrs. D. D., a primigravida, aged 24, was admitted to the Queen Elizabeth Hospital at 8.30 p.m. on October 12th, 1945, as an emergency.

The last period was on January 4th, 1945, so that she was due to be confined on October 11th, 1945. She had attended her antenatal clinic regularly, and had been normal until 1 week previously when she had noticed that her left leg was giving way. She called in her own doctor and was told to stay in bed. Her legs became progressively weaker. On questioning she admitted that she had a slight cold at that time.

She was sent to the Emergency Hospital, where she had booked to have her baby, on October 8th. The weakness progressed, and by the 10th she was unable to sit upright, collapsing when put on the bedpan. On the 12th her condition deteriorated, and she was transferred to this hospital.

On examination she was deeply cyanosed and her alae nasae were working.

Cardiovascular system. Heart normal; pulse 120. Her blood-pressure was not taken as her condition was too poor to delay.

Respiratory system. Very few breath sounds; intercostal muscles not working.

Abdomen. The uterus was enlarged to the size of a full-time pregnancy. The foetus presented as an extended breech, the presenting part being above the brim. The foetal heart rate was 90.

Central nervous system. Only a very rapid examination was made owing to the patient's poor general condition. Knee jerks and plantar reflexes were absent. Power appeared to be absent in the left arm, almost absent in the legs and only diminished in the right arm. The erector spinae muscles were not acting. There was no complaint of pain, but by this time the mental condition was becoming confused; the woman by then was unable to co-operate, and was rambling in her speech. A tentative diagnosis of either peripheral neuritis or infantile paralysis was made.

Progress. As the patient's condition was visibly deteriorating she was put into an iron lung (Nuffield pattern). After about 20 minutes her colour changed to pink. She remained confused for another 1½ hours, after which her mental condition began to improve considerably. She was unable to swallow although she could speak clearly.

After another hour she complained of abdominal pain and in due course labour was definitely established. The pulse was then 156, foetal heart 120, and the patient exceedingly frightened.

It was thought unlikely that she would survive, but she was so distressed that it was decided to deliver the living and apparently normal baby by Caesarean section at once.

Operation. October 13th, 2.30 a.m. Premedication. Atropine g. 1/100. Anaesthesia was induced with the patient still in the iron lung by means of cyclopropane and oxygen given in a Mushin closed circuit apparatus. An intratracheal tube was passed. She was then removed from the iron lung and a classical Caesarean section was rapidly performed. The usual dressing of gauze and wool covered by elastoplast was applied, and a self-retaining catheter inserted. A lumbar puncture was performed while she was under the anaesthetic. The anaesthetic had been continued with cyclopropane and oxygen, controlled-respiration technique being used during the whole of the time that the patient was out of the iron lung. The patient was returned to the iron lung and allowed to recover consciousness.

The baby was a normal, healthy male infant who has progressed in a completely satisfactory way.

Progress. (*a*) *The obstetric aspect.* The patient was completely conscious by 4.30 a.m. and her general condition was fair. She was complaining of pain over the wound, and the lax abdomen was seen to be moving up and down with the pressure changes in the iron lung, so a tight binder was applied. The general condition improved throughout the day, she took fluids well and secreted normal urine; pulse rate 108.

On the following morning, October 14th, she began to vomit slowly and continuously, and her pulse rose to 160. The abdomen was distended and tender. The stomach was aspirated, 12½ ounces of fluid being withdrawn, with a lot of wind. A flatus tube was passed without result. The abdomen, although distended, became soft and the pain was relieved. The patient complained constantly of thirst, and could not be quietened with sedatives. The thirst was so distressing that it was decided to attempt to put up an intravenous saline drip. A canula was inserted into the internal saphenous vein, and normal saline given as a continuous drip. The condition again improved, the thirst was quenched, the pulse came down to 128 and she passed urine. Drinks were recommenced that evening, but a 5 per cent glucose drip was continued for 48 hours. There was no further vomiting.

Oestradiol benzoate, 50,000 units was given to suppress lactation.

The bowels remained confined until a spontaneous evacuation on the 7th day. A soap enema was given on the 8th day. There was some difficulty in dealing with the constipation, but regular actions were established by the 12th day.

The wound healed satisfactorily, the stitches were removed on the 10th day. There was no pyrexia; the lochia was rather scanty throughout.

Nursing difficulties were great as the woman had to be drawn out of the lung for any attention. She was unable to breathe much by herself although encouraged to do so as much as possible, someone standing by to give artificial respiration when she gave up. At first she could stand being out for only 3 to 5 minutes at a time, becoming cyanosed and terrified quickly, so that nursing attention was confined to releasing the catheter and attending to pressure points twice daily.

F

On the 3rd day she was able to stay out for 20 minutes on end, on the 8th day 1½ hours, and on the 12th day for 10 hours.

(*b*) *The medical aspect.* The lumbar puncture performed at operation gave the following results. Pressure normal, with normal dynamics and Queckenstedt.

Biochemistry. The fluid contained a white coagulum. It was centifruged and the clear and colourless supernatant fluid used for analysis. Protein content: 86 mg./100 ml. Sugar content: 75 mg./100 ml. NaCl. content: 775 mg./100 ml. Globulin: Pandy, plus. Nonne-Apelt, trace. Urea content: 68 mg./100 ml. Lange: 0011000000.

Wassermann reaction. Negative.

The patient was examined by the honorary physician on October 18th. *Legs.* Quite good movements at ankles and toes, rather weak at hip and knees. Knee jerks practically absent; plantar reflexes, both flexor; sensation to pinprick normal.

Abdomen. Upper intercostal muscles being employed; diaphragm apparently not working; sensation to pinprick normal where tested.

Arms. Power: very weak and more so on the left. Left flexion and extension very weak at elbow. Right: flexion fair at elbow; extension, weak. Left shoulder: Abduction absent. Right shoulder: Abduction very weak. Left shoulder: Adduction poor. Right shoulder: Adduction about the same. Reflexes: Biceps—right, plus; left, absent. Supinator—right, plus; left, absent. Triceps—both absent.

Sensation to pinprick: Apparently some numbness at ends of fingers.

Cranial nerves. Face, no asymmetry; eye movements normal.

Diagnosis. Anterior poliomyelitis.

Subsequently the patient had some progression of the weakness of her legs particularly affecting dorsiflexion of the right foot. She remained in the iron lung until November 21st, 1945, when she was removed and showed poor respiratory movements, mainly diaphragmatic, with no power in her abdominal muscles. She complained of tightness of the chest and showed a slight degree of impairment to percussion at the right base. Penicillin and sulphonamide were commenced and penicillin was continued until December 20th.

·Subsequently she had periods of improvement in her ability to breathe, with periods of deterioration. She was in and out of the iron lung several times and had another course of penicillin for her chest condition. At about the middle of January. 1946 she began to develop signs of consolidation of the left base, which were shown on X-ray, and, on the whole, she deteriorated.

She was returned to the iron lung on January 23rd, and had a course of sulphonamides, which reduced her temperature, and gradually she again improved until she was having increasing periods out of the respirator, with a maximum of 4 hours.

During the time she was in hospital she had massage and breathing exercises when her general condition was suitable. The condition of the lesion of the central nervous system became static and she had great weakness of all limb muscles, as well as the muscles of respiration.

She was discharged to the hospital of St. Cross, Rugby, on February 27th, 1946. The following report was received from Rugby .on November 21st, 1946: " The patient has recently been discharged from hospital and is now ambulant, wearing a posterior spinal support. The abdominal and spinal muscles are still very poor, and are not likely to make much further recovery. She is, however, able to walk about and do a certain amount of her own housework."

The following points are interesting from the obstetric point of view.

(1) The onset of labour. This commenced quite soon after the patient was put into the iron lung. May not the rhythmical pressure changes have helped to stimulate the uterus at term, resulting in the onset of labour ?

(2) The method of delivery. Once in labour it was necessary to deliver the patient. The alternatives were Caesarean section, or to allow the cervix to become fully dilated and then deliver vaginally under anaesthetic, the patient being removed from the iron lung when anaesthetized. The former method was. chosen in view of the possible effects of labour on a patient in such poor general condition, the distress the patient already felt in being placed in the lung, and the unengaged breech presentation in a primigravida.

(3) The vomiting may have been encouraged by the negative pressure produced in the lung. The intravenous drip ran well in spite of this. The lung was kept working at a rate of 2 respirations per second, the pressure changes varying from + 18 to - 18 ml. water.

(4) The absence of any other postoperative complications in a patient nursed flat on her back without any attention being given to her bowels for a week.

SIR JOSEPH BARCROFT

Obituary

SIR JOSEPH BARCROFT

C.B.E., M.A. (Camb.), D.Sc., Hon. M.D., Hon. F.R.C.O.G., F.R.S.

SIR JOSEPH BARCROFT died suddenly at Cambridge on March 21st. He was 74 years of age. His life had been devoted to research in problems of physiology, nutrition and veterinary science. Though he was not a medical man much of his experimental work was done on human subjects and the results of his investigations have had far-reaching effects on the practice of medicine.

Joseph Barcroft was born on July 26th, 1872, the son of Henry Barcroft, D.L., of Newry, Co. Down. He was educated first at Bootham, the Friends' School, at York, and later at the Leys School, Cambridge. He entered Kings College, Cambridge, where he became a prizeman and exhibitioner in 1894. He took a first in both parts of the Natural Science Tripos and graduated in 1896. In 1900 he was elected to a fellowship in his own college and in 1910 became a Fellow of the Royal Society. Under J. N. Langley he held the University readership for a few years until in 1925 he succeeded to Langley's chair. This he held for twelve years. Unwilling to retire, he continued his investigations and turned at this time to a study of pre-natal physiology. In 1941, when he was nearly 70 years old, he accepted the directorship of the unit of animal physiology for the Agricultural Research Council. He held this post until his death. In these latter years he attacked problems in animal biology with the same enthusiasm as he had used in human physiology and with equally important results.

The work which will be associated with his name above all his other accomplishments is that relating to respiration. His work on the oxygen carriage of the blood is classical. Against strong opposition he maintained his theory that the passage of oxygen through the alveolar epithelium is a simple physical process. When experimental proof was necessary he did not hesitate to expose himself for several days to reduced oxygen pressure in a glass box in his laboratory. The question of altitude effects led him to organize an expedition to the Andes to study the condition at first hand.

His later work included a study of the function of the spleen, in respect to blood storage. From this he became interested in blood volume, which carried him on to the study of foetal circulation. He investigated the oxygen supply to the foetus in utero. Most of his work was done on foetal sheep. He showed that in these animals there is a relation between maternal nutrition and foetal development. Observations on human embryos were included in this work.

During the two World Wars he served in an advisory capacity to the War Office as a member of the Army Medical Directorate. He experimented with poison gas to deter-

mine its suitability for chemical warfare and in many other ways served the Allies.

He was knighted in 1935. Honorary degrees from universities at home and abroad were heaped upon him. In 1943 he received the Copley Medal—highest award of the Royal Society. In 1944, in recognition of his outstanding contributions to pre-natal physiology, the Royal College of Obstetricians and Gynaecologists elected him to its Honorary Fellowship. Until his death he was Chairman of the Nutrition Committee of the College.

He was simple, kind and sincere. Through his encouragement of the work of younger men he influenced contemporary physiology the world over. His students represented many countries. He wrote simply and spoke convincingly. His work showed characteristic enthusiasm to the end. He died while returning home from his laboratory.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A Meeting of the Council was held in the College House on Saturday, January 25th, 1947, with the President, Mr. William Gilliatt, in the Chair.

The following were admitted *in absentia* to Membership of the College:

Ian Brandon Ewart.
Goeffrey Jasper St. Clair Fisher.

The following candidates were elected to the Membership of the College:

Duncan Ballantine.
Margaret Rosalind Biggs.
William Stewart Campbell.
Henry Vincent Corbett.
John Barr Cochrane.
Sidney Joel Cohen.
George Laurence Daly.
Albert Davis.
John Roscoe Dickinson.
Bessie Dodd.
Morag Dods.
Ian Donald.
Robert Chalmers Gill.
Jean Lilian Hallum.
Arthur Jack Hardy.
Ronald Fox Lawrence.
Thomas Henry Lawton.
John Malcolm McBride.
Reginald Arthur Edward Magee.
Eileen Cathcart Miller.
James Duncan Murdoch.
Michael Kieran O'Driscoll.
Stewart Sandeman Favell Pooley.
Louis James Quinn.
Kathleen Mary FitzGerald Worrall.
James Lawrence Wright.

REPORTS OF SOCIETIES

ROYAL SOCIETY OF MEDICINE

Section of Obstetrics and Gynaecology
November 15th, 1946.

A discussion of "Stress Incontinence of Urine," held by the above section, was opened by Mr. Everard Williams, who reviewed at length the origin of this distressing symptom and the various methods of surgical treatment that had been tried in the past for its relief. He pointed out the necessity in any procedure for the elevating of the urethra at a point just as it left the bladder and described briefly the operation that he had practised with considerable success. This consisted in approaching the neck of the bladder from above and by suture approximating it to the fascia adjacent to the posterior surfaces of the pubic bones. Mr. Everard Williams was followed by Mr. Terence Millin. "Cases of stress incontinence," he said, "should be divided into four groups: Those with a congenital sphincteric weakness, post-puerperal cases which will frequently go on to spontaneous recovery or may be benefited by faradic stimulation, menopausal which may respond to hormone therapy, and lastly the commonly met with stress incontinence coming on some years after childbirth."

Cysto-urethroscopic investigation always revealed a patulous bladder neck, and at first he had always practised an intravesical operation whereby a wedge of tissue was excised from the posterior lip of the neck of the bladder. This was sometimes combined with the provision of a Goebell sling of ribbon catgut and such was the success that finally a decision was reached to discard the intravesical part of the operation entirely and to fix the neck of the bladder to the tendons of the recti close to the pubes, in an attempt to draw up and fix the ptotic structure.

Convinced that the essential requirement for cure was elevation of the bladder neck, he devised a "muscle hammock" or "sling" operation. The details of this operation are to be found in the published original paper. The underlying principle is the same as that used by Aldridge and others, in that the neck of the bladder is elevated by a fascial sling, originating at each end from muscle of the abdominal wall. In Millin's operation the whole rearrangement was effected through a single transverse incision of the skin and the fascial strips were cut transversely from the fascia in front of the abdominal wall muscles. He claimed good results, and many present hoped his good figures were more accurate in their estimation of success than were those he offered in his assessment of the cure rate (50 to 80 per cent) for stress incontinence by a simple anterior colporrhaphy. This figure was certainly too low in the opinion of subsequent speakers. Mr. Millin advised that whenever a vaginal wall prolapse was apparent the vaginal operation should first be tried, as when such a repair has failed to cure the incontinence he believed a sling procedure should be employed. He cited the results of 67 operations, with only one failure. Various details in after treatment were discussed.

Professor Chassar Moir followed and forthwith proceeded to challenge Mr. Millin in his statement that 40 per cent of cases of stress incontinence of urine are not cured by a simple operation from below. He said that in his opinion the Aldridge modification of the Goebell-Stoeckel operation deserved more attention than the mere mention that it had received so far. His introduction to this work was in 1929, when he saw Werner of Vienna perform the operation. Two narrow ribbons of fascia were dissected down from the anterior abdominal wall and left attached to the pyramidalis muscles. With the patient in the lithotomy position, exposure of the urethra and bladder neck was then made as in the orthodox colporrhaphy operation, and a tunnel opened up into the space of Retzius on both sides. The fascial bands were now pulled down by means of long forceps and were united under the neck of

the bladder. In 1942 Aldridge described a modified technique in which strips of fascia were dissected from the abdominal wall, above, and parallel to, the inguinal ligaments. These strips were left attached to the recti muscles about 1 inch above the pubes and brought down under the urethra as described above. A second modification was made by Studdiford, who first completed the vaginal dissection before the performance of the abdominal part of the operation. As in Millin's operation, the fascial strips were passed under the already mobilized urethra, brought up the tunnel in the fascia of the opposite side and sutured to the fascia of the opposite rectus muscle.

On the whole Professor Chassar Moir preferred the Aldridge technique. He did not approve of the wide opening up of the space of Retzius which was necessary in both the Studdiford and Millin operations. In the latter also there was a distinct risk of penetrating the vaginal wall or damaging the urethra or neck of the bladder.

Following the operation he advised catheter drainage for 10 days, during which time the patient is given sulphanilamide 0.5 g. 4 hourly.

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A meeting of the Section of Obstetrics was held at the Royal Society of Medicine, on Friday, January 17th. The subject under discussion was the management of the normal third stage of labour and the haemorrhage occurring during this stage. The opening speaker, Mr. J. D. S. Flew, postulated that, whereas attention had been given in recent years to the management of the antenatal period and to the first and second stages of labour, little change had taken place in the conduct of the third stage. He was not so much concerned as to how the obstetrician conducted this stage or how he dealt with cases of excessive haemorrhage, but rather with what was taught to medical students, and in particular to pupil midwives, who, when qualified, conducted 60 per cent of the midwifery in the country.

It was well known that a badly conducted third stage of labour could cause post-partum haemorrhage. Such bad conduct consisted usually of feeble attempts to express the placenta by massaging the uterus and pushing it downwards. If haemorrhage occurred Crede's expression was attempted, but usually failed. No other advice was given the midwife except that she should remove the placenta manually, and Mr. Flew doubted whether midwives could do this on their own. It would obviously be extremely dangerous in an already exsanguinated patient. The use of any oxytoxic drug was forbidden on account of the danger of the formation of a constriction ring. In 1935, in the Obstetric Unit of the University College Hospital, 0.5 mg. ergometrine was given intramuscularly to 500 consecutive normal cases as soon as the head was delivered. In no case was there any evidence of constriction ring, and in no case was a manual removal of the placenta necessary. He quoted Peel to the effect that a similar investigation had been carried out at King's College Hospital, using 5 units of pituitary extract. In these series constriction ring occurred twice. Mr. Flew did not suggest that the routine use of ergometrine during the third stage of labour should be taught. He had no hesitation, however, in advising that this drug should be given intravenously or intramuscularly in cases of haemorrhage during the third stage. Especially important, in his opinion, was it that much teaching should be thus revised when haemorrhage occurred in domiciliary midwifery, whether the case was conducted by doctor or midwife. The drug would control the bleeding, and the patient could be removed safely to a hospital where her general condition would be restored and the placenta removed manually under good conditions.

Mr. Gibberd believed that in the management of haemorrhage in the third stage of labour, in the practice of the midwife acting alone, routine treatment should not exceed 2 attempts at expression of the placenta. No one seriously expected a midwife to embark upon the operation of manual removal of the placenta, and there was every reason to believe that such heroic treatment, if adopted, was more likely to kill the patient than to save her life. It was therefore important to cease advocating such treatment, and more emphasis should be placed upon general measures for combating collapse that could be applied while proper assistance was awaited. Crede's method of expression failed because of a mechanical difficulty in securing a satisfactory grip of the uterus, or because of constriction ring, and he did not believe any other local treatment should be

attempted until an anaesthetist was available and adequate preparation had been made for manual exploration of the uterus. There was only one cause of mechanical difficulty in manual removal of the placenta, other than true placenta accreta, which condition he personally had not seen, and that was the constriction ring. He did not believe. in the condition of the " morbid adhesion " of part of the placenta nor could he support Mr. Flew in his proposition to advise the use of ergometrine in the third stage of labour.

Professor Lloyd in the main supported Mr. Gibberd. She emphasized that a distended bladder was one of the most common causes of delay in the third stage and, for the treatment of haemorrhage during the third stage, spoke in support of the " Flying Squad Service ", and the good work it was doing in Birmingham. A great majority of cases to which it was called were cases of this nature. This team of workers was always available, and on arrival at the patient's house concentrated at once on the restoration of the patient's general condition. Manual removal could usually be performed under satisfactory conditions, and ergometrine was not given before the placenta was delivered.

The last opener was Dr. P. Denham, who had just completed 3 years as Assistant Master of the Rotunda Hospital. He emphasized that at that hospital they saw no reason whatever to consider change of policy that has been in existance for some years in the management of the third stage of labour. That policy involves a careful watching of the patient's condition, and the absolute refusal to allow the attendant nurse or student to touch' or otherwise examine the uterus, in the absence of any untoward symptom or sign. When the umbilical cord lengthened and a small gush of blood indicated the separation and expulsion of of the placenta into the vagina, the Labour Ward Sister was allowed to feel the fundus, and to note the other signs of separation and expulsion. The catheter was then passed, and by gentle and intermittent pressure, the placenta and membranes were expelled intact from the vagina. If haemorrhage was noted without the signs of placental separation, a catheter was passed, the fundus massaged, and an effort was made to express the placenta by Crede's method. If this failed, the patient was anaesthetized and removal was attempted once more. Oxytoxic drugs were not given before the end of the third stage of labour. The results achieved can be tabulated as follows: out of over 7,000 deliveries manual removal of the placenta was necessary in under 1 per cent of the cases. Inversion of the uterus had not been seen in the Rotunda Hospital for at least 20 years.

Following the four opening speakers, many present at this very large meeting spoke. The points which attracted most attention were (i) that raised by Mr. Flew in advocating a revision of the management of haemorrhage in the third stage of labour, especially when it occurred in domiciliary midwifery, and (ii) the insistence from the Rotunda Hospital on the drastic revision of the teaching of the management of the normal third stage of labour in this country. On the first point, it appeared that the majority of speakers felt in the words of Professor Chassar Moir, that it was preferable to have a live patient with a retained placenta and constriction ring than a dead patient whose placenta had been removed.

March 21st, 1947.

Anaesthesia for Caesarean section.

Dr. Rufus Thomas (Croydon), said that he had used spinal analgesia induced with heavy nupercaine (Ciba) for almost all his Caesarean sections during the past 9 years.

The main objections to the use of spinal analgesia were briefly reviewed. One was that pregnant women near term were highly susceptible to cocaine products. Thomas pointed out that nupercaine, as a quinoline derivative, was not related to the cocaine group so this objection did not apply.

Another objection was that collapse and sudden death were liable to occur from sudden drop in blood-pressure, due to vasoconstrictor paralysis. This is avoidable, he maintained, by the following precautions: ephedrine should be given before operation; the position of the patient after injection of the spinal analgesic should be carefully adjusted so that the solution did not rise above the level of the eighth dorsal (which gave anaes-

thesia nearly up to the ensiform cartilage): by recording the blood-pressure throughout the operation and, if the systolic pressure fell to 90 mm. Hg., by injecting methydrine 15 mg. into the uterine muscle. This restores the blood-pressure up to or above normal very rapidly, by peripheral vasoconstriction. The other precaution was to avoid spinal analgesia in patients who had low blood-pressure or severe anaemia until their condition had been restored by blood transfusion and other means. Placenta praevia was the most common condition in this category. Thomas included in his numbers 58 cases of placenta praevia operated upon under heavy nupercaine spinal analgesia.

Cases of meningitis, some fatal, have been reported. This must be guarded against by the strictest precautions in the aseptic technique of preparation of needles, ampoules, syringes, hands of the anaesthetist and the back of the patient.

Headache was an objectionable postoperative complication, but could be minimized by using the finest spinal needle, keeping the patient flat for 24 hours after section and raising her to the semi-Fowler position very gradually. Headache is thought to be due to leakage of cerebrospinal fluid.

The advantages of spinal analgesia were stated to be:—

Injection is easy, the patient feeling nothing after the first prick of the needle.

The mother is fully conscious, hears her baby cry at birth and takes a lively interest in its condition and sex. She can be given drinks during and after operation, and can see her husband immediately.

The baby is completely unaffected by the anaesthetic. This is a great advantage in cases of foetal distress. Many infants cry before they have been completely extracted from the uterus.

The surgeon has the maximum of operative comfort. Relaxation is perfect, access to the lower segment being greatly facilitated. Uterine tone is good and bleeding minimal. Many operations are practically bloodless. The placenta often delivers itself.

The postoperative period is, apart from possible headache, very comfortable. Vomiting and distension are rare, and chest complications practically non-existent.

Thomas gave the following figures:—

No. of sections	No. of infants	Infant losses	Infant salvage, per cent
346	350	12	96.5

There was no maternal mortality, either under or due to the spinal analgesic.

Disproportion was the chief indication for operation; 58 cases of placenta praevia were operated upon.

Forty-one cases were operated upon twice, and 5 thrice, under spinal analgesia.

Thomas is of the opinion that spinal analgesia is safe for cases requiring Caesarean section, provided that proper precautions are taken. Women with cardiac decompensation are unsuitable.

Mr. Peel (London): My contribution to the discussion is a small series of cases of Caesarean section performed under caudal anaesthesia.

Fifty entirely successful operations have been done at King's College Hospital, with no maternal mortality, and no abnormal morbidity. No serious complications occurred attributable to the anaesthetic agent. All the babies were born alive. Three died during the neonatal period for reasons quite unconnected with mode of delivery or anaesthetic agent.

The advantages of regional block, achieved by either spinal or caudal anaesthesia, are that narcosis and anoxia of the foetus, invariable to a greater or lesser degree with all forms of inhalation anaesthesia including nitrous oxide and with intravenous anaesthesia are avoided. Caudal anaesthesia obviates the inherent dangers of spinal anaesthesia, to which the pregnant woman, in the experience of the majority, is particularly susceptible.

Technique consists of the injection into the sacral hiatus of 50 to 100 ml. of metycaine (1½ per cent) in divided doses—10 ml to 30 ml. and subsequently 10 ml. to 20 ml. depending upon the rapidity and extent of the development of anaesthesia. It takes 20 to 40 minutes from the initial injection before full anaesthesia is established. Slow injection of the fluid is necessary to prevent nausea, vomiting and drop in blood-pressure. Premedication is best avoided from the point of view of the baby, and no premedication is better than partial and inadequate premedication from the mother's standpoint. Patients with low blood-

pressure and recent haemorrhage are unsuitable, but otherwise the field of choice is wide and varied. It is particularly suitable for Caesarean section in the diabetic patient operated on before full·term. Haemorrhage is minimal and makes the operation safer for mother and child. Postoperative complications are minimal. The method is limited by difficulties in technique. Failure is always due to inability on the part of the anaesthetist to insert the needle into the sacral canal, due to anatomical abnormalities (10 per cent), obscuring of the bony landmarks by adipose tissue or oedema, and inexperience of the administrator.

Mr. Mackintosh Marshall (Liverpool) recalled that he had written something on this subject in 1939. There were still the 3 main anaesthetic groups —inhalation, spinal and local—though to these must now be added intravenous methods with or without the addition of curare. Though he had greatly increased his experience in all these methods there was nothing he would like to retract while there was much that he would heavily underline. Some people were already maintaining that pentothal-curare-cyclopropane was the answer to this problem. In one obstetric unit for which he was responsible this combination was being used, so that he might eventually learn its good and bad points. In the meantime it must be acknowledged that these three were highly potent drugs and, now that curare was available to all, he experienced a certain degree of apprehension for the future. In this regard a dictum of Beecher's (*J.A.M.A.*, 111, 122. 1938) should be borne in mind: " Whenever an anaesthetic agent has enough good qualities to get it past an early trial period, it seems to take about ten years to evaluate its bad effects."

There were reasons why most of the inhalation methods were unsatisfactory and even dangerous: (1) A minimal amount of pre-operative sedation often contributed to accidents during induction, such as vomiting, laryngeal spasm, etc. Aspiration pneumonia was not extremely rare and there were fatalities. If a state of anoxia arose in the mother it was transmitted to the child with extreme rapidity and atelectasis or even a stillbirth or neonatal death could result. (2) The action of inhalation anaesthetics on uterine tone was often unfavourable but could usually be counteracted by timely and adequate administration of oxytocic drugs. (3) If for any reason the delivery of the child

was unduly delayed, the foetus became anaesthetized and resuscitation might be difficult. If to this were added the shock of a difficult extraction, the child might succumb. Admittedly in the perfectly sound woman, operated on before the onset of labour, the above dangers, while real, were not likely to occur often with the expert anaesthetist.

But when labour had been prolonged, when poor uterine action had been a prominent feature, when large amounts of sedatives had been used, when the membranes had been ruptured many hours, if the foetus were premature, if moulding were extreme or a large caput were present or there were frank signs of foetal distress then one or other of these dangers was much enhanced, and he believed general anaesthesia was absolutely contra-indicated. The delayed emptying time of the stomach in labour had always to be remembered, and the nourishing draught of soup at noon was often returned into the anaesthetic mask in the evening.

The choice then lay between spinal and local anaesthesia. About spinal anaesthesia he would only say that it was practically ideal except in one respect —collapse or even death seemed to occur more often in Caesarean section than in any other abdominal operation for which it was used. Obstetricians were divided into 3 groups on this question; one had experienced fatalities and condemned spinal anaesthesia; another had neither experienced fatalities nor believed that they did or ever need occur; while a third, among whom was the speaker, firmly believed in this special risk and, further, that it was not always preventable. He still used spinal anaesthesia in a number of patients, always when he did an extraperitoneal section, in patients in whom special technical difficulties could be foreseen and, finally, in large or obese women whom he had found supported spinal anaesthesia extremely well. He had never seen spinal anaesthesia have the slightest adverse effect on the foetus.

However, he was still unable to deny the evidence of his eyes—local anaesthesia was safest for the transperitoneal lower segment operation. All the regrettable incidents which he had encountered during a long experience were associated either with inhalation or, but to a much lesser degree, with spinal anaesthesia. At least 6 out of 10 patients would support this method very well indeed. The remaining 3 or 4 demanded something

more, and with these it was the speaker's practice to open the abdomen under infiltration alone and to complete the delivery and operation quickly under a small dose of pentothal. It was, nevertheless, unlikely that many obstetricians would extend this form of anaesthesia to the majority of their patients. Yet there were certain conditions and circumstances in which safety of mother and child could be properly preserved only by the use of local anaesthesia, these were heart disease, diabetes, pre-eclampsia, most cases of antepartum bleeding, the premature child, and the case of the " very important baby ". Pre-operative sedatives should not be given. Local anaesthesia is of as much importance to the child as it is to the mother. It promises the best oxygen supply in the mother's blood so long as the baby is dependent on the placental circulation. It was often forgotten that the expectant mother was on the whole a most reasonable person. With simple and honest explanations her confidence could be won and she would no longer insist that delivery, whether vaginal or abdominal, should be entirely free from pain or discomfort.

Dr. Lloyd-Williams (London) gave a brief résumé of the methods used in the Obstetric Department of the Royal Free Hospital since 1928. She stressed the importance of complete confidence and co-operation between surgeon and anaesthetist. After a considerable trial of spinal analgesia, the method being used for some times as a routine in the Department, she does not advocate its use for the normal case. With the introduction of intravenous anaesthetics, and the light plane of anaesthesia usually required, she does not consider it justifiable to use a method which may involve apprehension and mental strain on the part of the patient.

Dr. Massey Dawkins (London): Epidural analgesia for Caesarean section possesses all the advantages of spinal analgesia without any of its disadvantages. There is no danger of meningitis or nerve lesions, fall of blood pressure is much less

and there is no headache. Patients are able to assume Fowler's position immediately on return to the ward and there is prolonged freedom from post-operative pain, in some cases for as much as 24 hours. The nursing staff much prefer it to any other form of anaesthesia. Pethidine 100 mg. is given 1½ hours before operation and this is repeated ¾ hour before. If there is any suspicion of foetal distress, this is omitted. Nupercaine 45 ml. of 1/600 solution is injected into the epidural space between the 1st and 2nd lumbar vertibrae, the patient is placed in 10° Trendelenberg position for 25 minutes and then the operation is commenced. Owing to the occasional failure of the anaesthetic to affect the touch sensation, some patients may require gas and oxygen, but if the difference between touch and pain is explained to the patient this is rarely necessary. In a short series of cases carried out in the Obstetric Department of the University College Hospital the results were uniformly satisfactory and there were no complications of any sort.

Dr. J. N. Cave (London): There was always some difficulty in pursuing a line of inquiry satisfactorily owing to the prejudices of surgeons, but, so far, results obtained seemed to show the following advantages and disadvantages of using a spinal anaesthetic for Caesarean section, especially the lower segment operation.

From the foetal point of view—the foetus unaffected by any drugs cries readily as soon as born, whilst in a large percentage of operations under inhalation anaesthesia there is difficulty with the infant for some time.

From the surgeon's point of view—he can proceed at his own pace, there being no need to hurry; the uterus contracts well and postpartum haemorrhage does not seem to occur, whereas after an inhalation anaesthetic sometimes the uterus is inclined to go slack. The main disadvantage is that this contractibility of the uterus sometimes makes the delivery of a large head somewhat difficult.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

A meeting of the Society was held in Manchester on January 3rd, 1947.

Dr. W. Calvert described a case of Rh iso-immunization treated by hysterotomy and sterilization, and asked the Society if it approved the course adopted.

Mrs. L., aged 41, had a child in 1927 which was alive and well. In 1929 she had a stillbirth at term; details of the foetus were not available. In 1931, 1934 and 1936 there were stillbirths between 6½ and 8 months, and all showed hydrops foetalis. In 1941 a pregnancy had been terminated at 3 months because of the previous history and without investigation.

The speaker first saw the patient in January 1946, when she was 3 months pregnant. Specimens of blood from Mr. and Mrs. L. were sent to Dr. F. Stratton, who reported that Mrs. L. was Rh negative and that there was a very-high antibody titre in her serum. The father was homozygous Rh positive. His children, therefore, would be all Rh positive and would suffer from haemolytic disease, which would be severe because of the high concentration of antibodies. In view of this, hysterotomy and sterilization were carried out in February 1946, removing two foetuses.

Dr. Stratton reported on the foetuses:

" (i) Length 74 mm. Rh positive.
   (ii) Length 78 mm. Rh positive.

" It therefore appears that these children would have been affected as suggested. The mother is Rh negative and has antibodies in her serum . . . I might add that the cells of these early foetuses show strong sensitivity.'

Dr. Calvert summarized that if a mother has had hydroptic infants and the father is homozygous there will be no more living children of that marriage. In putting the case before the Society, he wished not only to draw attention to this implication of recent knowledge, but also to find out if the Society approved the course adopted.

DISCUSSION

Dr. N. L. Edwards spoke on the question of re-marriage, and also told of a case in which a normal baby had been born following a previous pregnancy in which labour had been induced because of this condition, and twins had been born and developed icterus gravis and died. The father was said to be homozygous.

Dr. Rowarth suggested that the pregnancy should have been allowed to go on and the patient to have aborted or not as chance would have it, but if necessary to be sterilized later.

Mr. Snaith thought that the increased incidence of accidental haemorrhage was a point supporting Dr. Calvert's treatment.

Dr. Calvert, replying, thought that if there really was any chance of a normal child being born following such a history, then he would have to agree that sterilization was unjustifiable.

Prof. Daniel Dougal reported a case of torsion of an ovarian cyst associated with genital hypoplasia—bilateral aplasia of the paramesonephric or Müllerian ducts.

Miss K., aged 19 years, sought advice because she had not menstruated. Her vagina was absent, physique good, secondary sex characteristics well developed, but unattractive and dull mentally. She was not contemplating marriage and there was no need to construct an artificial vagina.

In addition to primary amenorrhoea, she complained of right-sided abdominal pain of sudden onset 3 weeks previously, which remained severe for a week, but was now much better though still troublesome.

Abdominal examination was negative. External genitals were normal. The hymen surrounded a shallow depression which represented that part of the vagina developed from the urogenital sinus. A cervix could not be palpated on rectal examination, but an elastic swelling the size of a goose's egg could be felt applied to the right lateral wall of the pelvic cavity. In view of the possibility of retained menses in one half of a double uterus the abdomen was explored.

The ovaries were well developed but longer than normal and their axes were directed downwards towards the corresponding internal abdominal ring, to which they were attached by a short length of ovarian ligament. The uterus was represented by a curved and flattened band of muscular tissue about a quarter of an inch wide lying beneath the peritoneum covering the posterior and lateral aspects of the bladder and terminating on each side at the internal abdominal ring immediately mesial to the ovarian ligament.

The Fallopian tubes were absent except for some fimbriae close to the upper pole of each ovary. Close to the fimbriae on the right side was a small cyst 1¼ inches in diameter, evidently an enlarged hydatid of Morgagni. The cyst was bluish-black in colour from torsion of its pedicle.

The right kidney of normal size lay beneath the

peritoneum covering the lateral wall of the true pelvis. It formed the swelling palpated on rectal examination. The left kidney was normal in size and position.

It seemed that the Müllerian ducts had remained in an extremely rudimentary state and there was no attempt at fusion except at their lower extremities. This may have been either the cause or the result of abnormal action of the gubernaculum, which had dragged its point of attachment to each Müllerian duct, i.e. the future uterine cornu, right down to the corresponding inguinal canal as occurs normally in the male.

Prof. Dougal had seen 2 other cases in which a similar failure of development had occurred unilaterally and the kidney was absent on the affected side.

Dr. C. E. B. Rickards described " Two cases of renal dystopia associated with gynaecological conditions."

CASE 1. A housewife, 32 years, healthy-looking, with normal menstrual history. She had one child aged 8 years, the confinement being followed by obstetric paresis. She complained of backache, yellow discharge, and dysmenorrhoea. Examination revealed an unhealthy cervix, an anteverted uterus lying to the right and irregularities in the posterior fornix. Diagnosis was made of endometriosis and chronic cervicitis.

She was admitted to hospital, examined under anaesthesia, and the abdomen opened. The right half of the uterus was normally formed, the left rudimentary. The right Fallopian tube and round ligament were normal. The right ovary contained a follicular cyst the size of a golf ball. On the left a fibrous hypoplastic tube ran into an eminence representing the left side of the uterus. The left ovary and round ligament were well formed. There was a marked degree of endometriosis in the recto-vaginal space. The left kidney lay in front of the sacrum.

Panhysterectomy with right salpingo-oöphorectomy was done. The left ovary and rudimentary Fallopian tube were not removed. Recovery was uneventful.

Radiological examination showed a right kidney with slight dilatation of the pelvis in normal position. The left kidney was overlying the right

sacro iliac joint. Tests of renal function did not show abnormality.

CASE 2. An unmarried woman, aged 36 years, who complained of heavy periods every 3 weeks for the past 3 months and dragging pain in the right side during menstruation for 6 months.

Examination revealed a fibroid in the uterus and a haemoglobin of 54 per cent.

Laparotomy revealed the uterine fibroid and a retroperitoneal mass anterior to the sacrum. The renal pouches were empty.

Panhysterectomy was performed.

Subsequent radiological examination showed the left kidney pelvis lying over on left wing of the sacrum, and the right lying in the hollow of the sacrum.

Dr. Rickards commented that according to Young any kidney out of its normal position may be referred to as dystopic. An ectopic kidney implies that the condition is congenital. According to Fowler, three types are recognized, the commonest being unilateral ectopy, the next being crossed ectopy, and the rarest being bilateral ectopy. According to Eisendrath, only 33 cases of bilateral ectopy had been reported up to 1937. The congenitally displaced kidney usually has a short ureter, has little or no fatty covering, and derives its blood supply from many vessels arising from the aorta and iliac arteries. Most of these cases are asymptomatic and operative treatment is not called for.

Mr. G. McIntosh Marshall read a paper on " Fascial Slings—the direct suprapubic route ".

Mr. Marshall stated that the anatomy is constant but the technique can vary in many details. Obesity does not render the operation more difficult, but previous lower abdominal incisions may cause a little embarrassment.

This operation seems to be better than the Aldridge operation in 4 ways : 1. The route is entirely abdominal, there is therefore less risk of sepsis. 2. The duration of the operation is less. 3. The sling supports a higher portion of the urethra—the urethrovesical junction. 4. The sling has its origin in an active muscle slip. On the other hand, this operation is not associated with repair of the anterior vaginal wall; but the clinical state of the majority of patients selected does not show

need for this. Mr. Marshall doubts whether the usual vaginal procedures possess very enduring features, the tissues are so tenuous and indeterminate.

The musculofascial sling works by elevating and angulating the urethra and, indirectly, the urethrovaginal septum and the anterior vaginal wall; it compresses the urethra and this effect is increased by the expiratory movements of the abdominal wall whether of normal respiration or more violent coughing or sneezing. All these actions are demonstrable during the operation. How long the fascial sling persists as a tendon moving in response to its muscle is not yet known, but so long as the static effect of the sling persists the result will be satisfactory.

In selecting patients Mr. Marshall had not limited his choice to those in whom other plastic methods had failed; he had used it as a primary procedure in a few cases complaining of partial or complete incontinence where there had been little or no evidence of prolapse. The immediate results had been most gratifying.

With epidiascope and cinematograph Mr. Marshall demonstrated the musculofascial slings which he had devised and employed. Through a Pfannenstiel incision a " bucket-handle " of fascia about one inch in width was raised, each end remaining attached to a fleshy slip of the external oblique muscle of the corresponding side. The " bucket-handle " was then split from one extremity to the other so that each limb of the eventual sling would be equal to the full length of fascia originally raised. To the ends of each of these fascial strips ligatures were attached.

The urethra with its catheter *in situ* was then raised and steadied with specially devised forceps, while a Bonney-Reverdin needle (aneurysm pointed) was passed beneath it through the tissue of the urethrovaginal septum. The ligature was drawn back with its attached fascial strip. The needle was reversed and the other strip similarly brought into position, the loops of the sling thus crossing beneath the urethra. The recurrent loops were then attached to the rectus fascia.

The proximal loops of the sling could be brought to the urethral region by different routes: (1) behind the rectus muscles; (2) through the centre of the rectus muscles as suggested to him by Mr. Charles Read, of London; (3) medial to each rectus muscle; this is not recommended.

Recently Mr. Marshall had devised a much simpler operation whose immediate effects were excellent. A transverse strip of fascia was completely detached; one end of this was passed through the centre of the left rectus muscle a short distance above its origin, underneath the urethra and up through a corresponding point in the right rectus muscle. The ends were then overlapped in front of the muscles and firmly joined with three silk sutures; or the fascia itself could be knotted if this was preferred. Such an operation could be rapidly performed. Having a muscular support, the sling was less rigid than that of Aldridge or slings which had their origins and insertions in aponeurosis. He now proposed to give an extended trial to this operation.

Mr. Jeaffreson asked whether any difficulty had been experienced in passing the musculofascial sling in cases having had previous vaginal operations. Dr. Racker asked if the operation might produce residual urine as a permanent factor.

Dr. Hunter said that where similar operations had been done in large numbers fistulae had been produced, suprapubic drainage had been necessary, and in some a basal cystitis had occurred.

Mr. Marshall replied that he had not found difficulty in passing the musculofascial slings. The operation did produce residual urine for as long as 10 days. He left a catheter in the bladder for some days. A coudé or bi-coudé catheter was needed if further catheterization became necessary.

REVIEW OF CURRENT LITERATURE

INDEX

The Journal is fortunate in being able to run this Index in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Index will, however, contain in addition abstracts of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstractors in foreign languages and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstractor will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

ANATOMY

87. Morphology. and Distribution of the Uterine Nerves. (Osservazioni sulle caratteristiche morfologiche e distributive dei nervi dell'utero della donna.)

By N. DAMIANI. *Boll. Soc. ital. Biol. sper.,* **22**, 216–219, March 1946. 2 figs., 4 refs.

The author has studied the innervation of different segments of the uterus as to their possible influence on parturition. He used the Bielschowski-Gros silver method and Ruffini's gold impregnation. The minute details of anatomy cannot be given here. Suffice it to say that the fibres pass along the lateral borders upwards and downwards from just above the fornix and also penetrate transversely into the musculature. The majority of the fibres are non-myelinated, and many of those just above the fornix penetrating the uterus possess ganglia which are seen also on fibrils among the superficial muscle bundles of the cervix (intrauterine ganglia). Fibres in the parametrium also show ganglia (extrauterine ganglia) at the side of the fornix and cervix. The ganglia contain large multipolar and many smaller, rounded cells. Also, sympathetic fibres are furnished to the vessel walls.

The cervix is more abundantly supplied with nerves than is the body of the uterus and the nerve bundles are thicker in the former; those to the latter are not sheathed as a rule; a few myelinated may be seen among them, but the sheath is very thin and delicate. In the intravaginal part of the cervix is a diffuse non-myelinated network.

The author states that the interpretation of his findings are largely hypothetical, but he suggests that orthosympathetic and parasympathetic nerves each play their part; that the orthosympathetic transmit the main motor stimuli to the whole uterus, while the parasympathetic have an accessory excito-motor function, curbing and regulating not only the uterine contractions, but also, and even to a greater degree, controlling dilatation of the cervix.

. *H. Harold Scott*

88. A Discussion of Pelvic Variation and a Report on the Findings in 100 Negro Women.

By H. THOMS. *Amer. J. Obstet. Gynec.,* **52**, 248–254, Aug. 1946. 2 figs., 11 refs.

Thoms adds to the records of his radiological study of the pelvis, male and female, by reporting his findings in 100 adult negro women delivered of their first full-time child in the New Haven Hospital. The study includes two consecutive groups of 71 and 29. As with other studies he has made, Thoms classifies the pelves into 4 groups: (1) dolichopellic, in which the antero-posterior diameter of the inlet is longer that the transverse; (2) mesatipellic, in which the 2 diameters are equal or the transverse is not more than 1 cm. longer than the antero-posterior; (3) brachypellic, in . which the transverse is between 1 and 3 cm. longer than the antero-posterior; (4) platypellic, in which the transverse is 3 cm. or more longer than the antero-posterior.

In the 100 negro women the incidence of each group was as follows: dolichopellic, 29 per cent; mesatipellic, 43 per cent; brachypellic, 25 per cent; platypellic, 3 per cent; while the incidence in 500 white primigravidae was: dolichopellic, 22.6 per cent; mesatipellic, 46.6 per cent; brachypellic, 28.8 per cent; platypellic, 2 per cent. The author concluded that the female pelvis in both white and black races is subject to considerable variation, and that the tendency for the pelvis to retain its foetal and infantile general characteristics is favourably influenced by nutrition. On the importance of the effect of nutrition on. the pelvis he agrees with Nicholson, Breus, Kolisko, Allen, and others.

J. Stallworthy

PHYSIOLOGY

89. Adenosine Triphosphatase Activity of Lutein and Ovarian Tissues and Weight of Corpora Lutea during the Reproductive Cycle of the Rat.

By C. BIDDULPH, R. K. MEYER, and W. H. McSHAN. *Endocrinology,* **38**, 358–367, June 1946. 4 figs., 13 refs.

Adenosine triphosphatase plays a major part in the energy exchanges of muscle and other tissues during glycolysis. By analogy, investigation of the adenosine triphosphatase activity of corpora lutea and other parts of the ovary during the oestrus cycle, pregnancy, and lactation may help to determine the functional activity of these tissues.

The dissected and weighed corpora lutea and ovarian residue were placed in tapering tubes fitted with ground-glass rods for homogenization and glass-distilled water added to make a 1 per cent homogenate. The adenosine triphosphatase

was determined by the method of DuBois and Potter (*J. biol. Chem.*, 1943, **150**, 185) with slight quantitative modifications, the volume of adenosine triphosphate and trichloracetic acid used was increased (0.2 ml. for 0.15 and 0.1 ml. respectively) and was made with an Evelyn photometer of the inorganic phosphate in 0.3 ml. of the digest supernatant diluted in 10 ml. The activity was expressed in units defined as the amounts needed to liberate 1 μg. of inorganic phosphorus from adenosine triphosphate in 15 minutes at 37°C.

The activity per milligramme of corpus luteum was slightly higher in dioestrus than in oestrus, remaining steady during pseudopregnancy and early pregnancy and rose before delivery, and this rise was continued during lactation (litters reduced to 6 young), reaching a maximum of about 300 per cent of the normal at the eleventh day of lactation. The corpora lutea formed immediately after parturition showed normal activity during lactation but increased activity after weaning on the twentieth day when oestrus recurred. The weight of each corpus luteum increased about threefold between the seventh day of pregnancy and delivery and thereafter fell to subnormal weights by the eleventh day of lactation. The postpartum corpora lutea did not increase in weight until after weaning. When the activity per corpus luteum was calculated its course paralleled the changes in average corpus luteum weight.

The rate of progesterone secretion, as suggested by the evidence of other authors, is apparently inversely related to the adenosine triphosphatase activity of luteal tissue; periods of high secretion (early pregnancy and lactation) are periods when low activity is found in the corpora lutea of pregnancy and of the postpartum ovulation respectively. There is similar evidence of inverse relations between oestrogen production by the ovarian residue and its adenosine triphosphatase activity; this was high in early pregnancy or pseudopregnancy, but fell before the recurrence of oestrus.

The range of activity per milligramme of fresh tissue was 7-25 units in luteal tissue and 15-20 units in ovarian residue. The average corpus luteum weights lay between 0.5 and 2.9 mg. Three rats were used for each determination, and individual variations were relatively great.

Peter C. Williams

PREGNANCY

NORMAL

90. The Elderly Primipara.

By F. BENJAMIN. *S. Afr. med. J.*, **20**, 674–682, November 9, 1946. 46 refs.

The author applies the term elderly primipara only to " a woman giving birth to her first viable child at the age of 35 or over "; he points out that the abnormalities to which the " elderly primipara " is especially prone do not make their appearance abruptly, but may be seen at any age over 25. While it is true to say that a proportion of elderly primiparae undergo an uncomplicated labour easily and normally, this state of affairs must be regarded as the exception rather than the rule. In the vast figures collected for New York State in a 3-year period, where a series of 255,727 cases of labour was available, the elderly primipara constituted 1.2 per cent of this figure and 3.2 per cent of all primiparae. Therefore, the elderly primipara figures in 1 out of every 100 cases with which the obstetrician has to deal. Since the incidence of women having their first babies at the age of 35 or over is greater among the well-to-do than among the working classes, it follows that a lower incidence will be found among hospital patients than in private practice. There is no doubt that the percentage of elderly primiparae delivered in hospital has steadily increased of late years, but this may be accounted for by contingent circumstances, and it may be taken that in general there is no absolute increase.

Again using the New York State series of cases, the author demonstrates that while the mortality rate for the whole of the series was 0.269 per cent that for the elderly primipara was 1.348 per cent —a figure nearly five times as high. The mortality curve mounts steadily and increasingly steeply as age advances. Infantile mortality, too, shows a marked increase with the increasing age of the mother. An infant mortality rate of 5.98 per cent for all cases from the New York State series compares with a rate of 11.48 per cent where the elderly primipara is concerned. The toxaemias of pregnancy, accidental haemorrhage, and placenta praevia—all factors directly affecting maternal and infantile mortality rates—are to be found far more often in the elderly primipara than in the primipara of younger ages. Abnormal presentations are 1½

to 3 times as frequent in the older age-group. Uterine inertia, especially when occurring in the third stage, is one of the greatest risks which the elderly primipara has to encounter.

The author advises that antenatal care of the pregnant woman at or over 35 years of age should include routine X-ray pelvimetry, special attention being paid to the assessment of the pelvic outlet. The type of cervix and vagina should also be determined. Because of the pernicious effect of fear—so common in elderly pregnant women—special attention should be paid to the psychological factor. Caesarean section, with its relatively high mortality rate, should be avoided wherever possible, and its use reserved for the genuine obstetrical indication. The only rational approach to the problem of delivery is through the careful study of each case, and even when delivery is safely effected the problems of the puerperium demand that unremitting care should be exercised.

F. L. Cary

91. Carbohydrate Content of Serum Proteins in Normal and Toxemic Pregnancy.

By B. LUSTIG and J. NOVAK. *Exp. Med. Surg.*, 4, 255–259, Aug., 1946. 18 refs.

Earlier investigation by the same authors has shown that hypoproteinaemia with decrease in the albumin-globulin ratio occurs in pregnancy and is particularly marked in the toxaemias. This has been regarded as the result of dilution of the blood due to water retention. The present paper describes qualitative changes in the serum proteins resulting from changes in their carbohydrate content estimated by the orcinol-sulphuric acid reaction. Globulin was precipitated by Kingsley's method, 15 ml. of 23 per cent sodium sulphate being added to 1 ml. serum in the presence of ether; the figures for globulin were calculated by subtraction of the estimated results of total protein and albumin. Eight normal non-pregnant women, 22 women during normal pregnancy, and 7 cases of toxaemia were investigated. Though total protein-carbohydrate was not significantly altered by pregnancy, the carbohydrate content of the albumin fraction was significantly increased in pregnancy. In toxaemic pregnancy protein-carbohydrate was increased both for the total protein and for the albumin and globulin fractions. Present results do not indicate whether this is due to

alteration in composition of known proteins or to the appearance in the blood of new serum proteins.

R. H. D. Short

92. Maternal and Foetal Tissue and Plasma-lipids in Normal and Cholesterol-fed Rabbits.

By G. POPJAK. *J. Physiol.*, 105, 236–254, Dec. 6, 1946. 11 figs., 21 refs.

93. Discussion on Water Metabolism in Pregnancy.

By W. H. NEWTON, G. W. THEOBALD and W. C. W. NIXON. *Proc. R. Soc. Med.*, 39, 558–568, July 1946. 33 refs.

Newton divides the water of the body into three compartments: intracellular water, interstitial (or tissue) fluid, and blood plasma. The intervening barriers are, respectively, the cell membrane and the capillary wall. The former is impermeable to the majority of ions; the latter is thought to be permeable to all constituents of the plasma except protein. The adjustment of exchanges between plasma and tissue fluids chiefly depends upon an adequate plasma protein concentration, but the mechanical factors of pressure within the capillary lumen and within the tissue spaces are also important. Varying permeability of the capillary membrane is another possible factor. The ion distribution of the tissue fluid and of the plasma are so nearly identical that they may be conveniently grouped together as the combined extracellular fluid, the volume of which may be measured by studying the degree of dilution of a measured amount of sodium thiocyanate. Blood plasma volume can be estimated separately by a similar technique, using Evans blue, which is not diffused through the capillary endothelium.

In pregnancy the combined extracellular fluid is increased. According to Chesley (*Amer. J. Obstet. Gynec.*, 1944, 48, 565) the average increase is 6.3 litres. Of this figure Chesley believes that the plasma accounts for 1.3 litres and the interstitial fluid for 2.5 litres. The remainder is included in the breasts, uterus, and products of conception. Newton examines these figures critically. He considers that since the normal ratio of interstitial fluid to plasma fluid is believed to be 4:1 an explanation is required for the apparent irregularity of division. Far from finding factors encouraging selective retention by the plasma, he points out changes operating rather in favour of an increased proportion of interstitial fluid, such as dilution of the plasma proteins, increased venous pressure in

the lower limbs (McLennan, *Amer. J. Obstet. Gynec.*, 1943, **46**, 63), and possibly increased capillary permeability. The reasons for water retention in pregnancy are obscure. Retention of sodium in the latter part of pregnancy occurs, but in such large quantities that, if osmotically active, it would require retention of a greater weight of water than the total observed weight gain. It is therefore apparent that at least a proportion of the retained sodium is osmotically inactive and hence caution is needed in attributing any portion of the water retention to this cause. Nevertheless it has been shown that during pregnancy administration of sodium chloride over a period of several days causes a weight gain which water balance estimations show to be due to water retention, and that subsequent withdrawal of the sodium chloride causes reduction of weight due to water excretion, Freyberg, Reekie and Folsome, *Amer. J. Obstet. Gynec.*, 1938, **36**, 200), while administration of oestrogens and progestogens can cause retention of sodium and water. (Taylor, Warner and Welsh. *Amer. J. Obstet. Gynec.*, 1943, **45**, 547).

G. W. Theobald states that excess tissue fluid can cause cerebral convulsions or oedema of the lungs, and the control of water balance is one of the most important functions subserved by the kidneys. The kidney shows a latent period before responding by diuresis to the absorption of water from the alimentary canal—a mechanism which may be explained by tubular re-absorption caused by posterior pituitary antidiuretic substance. Theobald examines the possible factors which may predispose to excessive water retention in the tissues in pregnancy. He agrees that the blood dilution allows of increased loss of fluid from the arterial end of the capillary loop, but that a correspondingly enhanced concentration of the plasma colloids at the other end of the capillary prevents any progressive loss of fluid to the tissues. Storage of sodium is not the sole or even the determining factor. The important causative agent is considered to be mechanical, increased venous pressure due to the weight and bulk of the pregnant uterus causing a general rise in the venous pressure throughout the body by the consequent restriction of diaphragmatic movement, and exercising a more direct action on the venous drainage of the lower limbs so long as the erect position is maintained. (McLennan, quoted by Newton, demonstrated significant increase in

femoral-vein pressure even in recumbancy.) Support for this idea is found in the well-known increased incidence of water retention in primigravidae and in cases of plural pregnancy, and in the fact that a postpartum diuresis occurs shortly after delivery, while the blood is still hydraemic and sodium retention still exists. Theobald admits the possibility that this may result from withdrawal of the sex steroids, but, in the absence of evidence of increased sex steroids in the blood of patients suffering from oedema, he prefers to accept the mechanical factor as more important. He also discusses the question of weight gain in pregnancy, the major portion of which he accounts for as follows:

(1) Products of conception ... 11.5 lb. (5.2 kg.)
(2) Uterus and adnexae ... 2.5 lb. (1.15 kg.)
(3) Breasts ... 3.0 ± 1 lb. (1.35 ± 0.45 kg.)
(4) Increased blood volume ... 2.5 lb. (1.1 kg.)
 ‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾‾
 19.5 ± 1 lb. (8.8 ± 0.45 kg.)

Another cause of weight increase is nitrogen retention equivalent to more than 6 lb. (2.7 kg.) of protein or to 30 lb. (13.5 kg.) of tissue. This last figure seems so unreasonable that it may be assumed that the nitrogen is not stored as protein. Additionally, a few pounds of fat are generally laid down around the hips and waist. Water retention may further contribute to weight gain. One extra litre may be retained in the tissues in normal pregnancy, and in abnormal pregnancy 2 further litres (3 in all) may be accommodated without producing oedema or other untoward symptom. The weight of this additional 2 litres is less than 5 lb. (2.3 kg.) and this figure is important in toxaemia of pregnancy, for, if warning of impending toxaemia is to be gained from weight records, the significant occurrence would be a sudden gain of up to 5 lb. (2.3 kg.) between the twenty-eighth and thirty-sixth weeks of pregnancy. Water retention greater than this would cause symptoms.

The occurrence of oedema is dependent on alteration of capillary permeability by malnutrition, chemical poisons, or physical injury. Malnutrition may indicate either the effects of local congestion (such as the stagnation of heart disease) or the local effects of general malnutrition (as in ankylostomiasis and beriberi). In such cases of increased

permeability of the capillaries the oedema fluid may contain considerable amounts of protein. Excessive water retention is best prevented by a well-balanced, easily digested, attractive diet, containing adequate amounts of first-class proteins, vitamins, and minerals; regular bowel action, sufficient exercise, and mental health are also essential. It is not necessary to restrict the intake of table salt or of sodium bicarbonate. The water balance may be restored by restricting fluid intake, by diuretics, and by increasing the periods of rest in the supine position.

Nixon discusses oedema in pregnancy with particular reference to the frequent occurrence of oedema in the absence of toxaemia and to the correlation between vitamin B_1 deficiency and pregnancy toxaemia. The importance of hypoproteinaemia in causation is emphasized. In prevention of oedema Nixon recommends a high-protein salt-free diet, and condemns the prescription of low-protein diets in the treatment of mild pre-eclampsia. Slight oedema will often disappear with alkaline medication. Diuretics such as potassium or ammonium chloride are permissible, but mercurial diuretics should be avoided. In more severe cases rest in bed is essential, and for 24 hours fluid intake should be restricted to 500 ml. of 30% glucose. Thereafter daily fluid intake should be adjusted to a total of 50 ml. less than the urinary output in the previous 24 hours, the diet (1,200-1,500 calories) consisting mainly of sugar, skimmed milk, vegetables, and fruit. Diuresis may also be encouraged by the intravenous injection at 6-hourly intervals of 50–100 ml. of 50% glucose solution. During diuresis it is desirable to administer a daily dosage of vitamin B_1 10 mg., vitamin C 300 mg., nicotinic acid 100 mg., and riboflavin 5 mg. In hypoproteinaemia advantage may be gained from plasma transfusion.   *W. I. C. Morris*

94. Composition of the Human Placenta. II. Lipid Content.

By J. P. Pratt, M. Kaucher, E. Moyer, A. J. Richards, and H. H. Williams. *Amer. J. Obstet. Gynec.* **52**, 665–668, Oct. 1946. 19 refs.

Lipids are important sources of nourishment for the growing foetus and, with the improved methods of analysis, it has been possible to determine the partition of the various lipid fractions in full-time placentas. Klaus emphasized that the different methods of preparing the tissue and the selection

and use of solvents in the extraction process explain the diverse results hitherto published. Higuchi found in full-time placentas 0.85 g. of fatty acids per 100 g. of fresh weight; if the placentas were thoroughly washed only 0.54 g. was found, indicating that one-third of the first value came from the blood present. Bienenfeld showed that the lipid content diminished as pregnancy progressed, and her comparison of placentas of 3 to 5 months with placentas at term indicated a decrease in total petroleum-ether extract from 8.6 to 4.4% of the dry weight. Total cholesterol dropped from 2.25 to 0.37% of the dry weight and cholesterol esters from 1.25 to 0.12%. Watanabe, in the developing human placenta, demonstrated a progressive fall in total cholesterol, total ether-soluble phosphorus, total lipids, and total fatty acids. He showed that, in terms of weight of the embryo, at the fourth month of development the fats and lipids of the placenta are present in greater quantity than at any other time. From these results Needham points out a similarity between the developing placenta and the developing hen's egg. In both there is disintegration of the lipid, releasing fatty acids, phosphorus, and choline. Evidence of important nutritional functions of the placenta has been contributed by Boyd and Wilson, who have demonstrated the passage of phospholipids, free cholesterol and cholesterol esters through the umbilical cord to the human foetus.

In the present investigation, the lipid distribution was determined in nine full-time placentas. The dried material was extracted with hot ethanol, then with ethyl ether. The final extracts combined represented approximately a 3 to 1 mixture of alcohol and ether and were analyzed for sphingomyelin, total and free cholesterol, galactose, and acetone-soluble glycerol. From the analyses the quantities of total phospholipid, choline phospholipid, cephalin, lecithin, cholesterol ester, cerebrosides, and neutral fat were calculated. The total lipid in the placentas averaged 12.36% of dry weight, and neutral fat 3.51%. The average essential lipid was then 8.85% (total lipid minus neutral fat) with total phospholipid composing 6.79% of which 2.26% was cephalin, 3.55% lecithin, and 0.98% sphingomyelin. Cerebrosides averaged 0.53%, free cholesterol 0.99%, and cholesterol esters 0.54% of the dry weight.

F. J. Browne

95. **Composition of the Human Placenta. III. Vitamin Content.**

By J. P. PRATT, C. RODERUCK, M. CORYELL, and I. G. MACY. *Amer. J. Obstet. Gynec.*, 52, 783–787, November 1946. 12 refs.

96. **Functioning of the Fetal Kidney as Reflected by Stillborn Infants with Hydroureter and Hydronephrosis.**

By L. J. WELLS and E. T. BELL. *Arch. Path.*, 42, 274–276, October 1946. 25 refs.

97. **Hypoxemia of the Fetus.**

By H. F. TRAUT. *West. J. Surg.*, 54, 379–383, October 1946. 6 refs.

The mechanism of the interchange of essential material between the foetal and maternal circulations is one of the most imperfect and, therefore, one of the most vulnerable that nature has produced. In the early stage of development this interchange takes place across the 2 layers of trophoblast, the villous connective tissue, and the foetal vessel wall. The disappearance of the Langhans layer later in pregnancy leads to a shortening of the distance between the circulation and makes the process easier at a time when the foetus is in greater need of nutritive elements and requires to excrete more waste products. The circulation of maternal blood through the intervillous spaces is extremely slow, giving time for the digestion and transmission of protein material. This stasis leads to low oxygen tension and makes the human foetus more vulnerable than any other mammal to any influence which affects a reduced oxygen tension. Compensatory mechanisms are the higher number of red blood cells in the foetal circulation than in the adult, and the greater efficiency of foetal homoglobin. Wislocki has shown that oxidative potentials may be available to the foetus from the anaerobic breakdown of glycogen. Despite these advantages the oxygen saturation of foetal blood constantly diminishes towards term, falling in the last 3 months from 50 to 28 per cent of saturation.

Haemovillous degeneration of the placenta with retroplacental clot formation (familial or toxaemic), anaesthesia and drugs, or maternal malnutrition may seriously impair the oxygen supply. Any of these conditions may be a possible cause of spastic paraplegia or of low-grade intelligence. Windle's experiments on animals support this hypothesis. Preston found that 97 out of 135 children who had been exposed to various degrees of hypoxaemia at or near term were suffering from serious difficulties of behaviour though of normal intelligence. The other 35 showed subnormal intelligence, or had locomotor difficulties or ataxia. Erythroblastosis foetalis may result in a similar clinical picture though of different aetiology. Premature separation of the placenta, and other accidents of childbirth such as prolapse of the cord, cord round the neck, and knots of the cord, while not causing foetal death, may damage the central nervous system from anoxaemia. In cyanotic conditions of the mother during pregnancy, an early recourse to oxygen inhalation may prevent foetal damage. Every effort, therefore, should be made by the obstetrician to protect the oxygen supply of the foetus.

D. M. Stern

98. **Further Observations on Prostigmine in Delayed Menstruation and Pregnancy.**

By D. PARRELLA. *West. J. Surg.*, 54, 397–402, October 1946. 1 fig., 8 refs.

In 1939 Reynolds demonstrated a rise in the acetylcholine content of rabbit uteri after the administration of oestrin to ovariectomized animals. The presence of acetylcholine in the uterus causes hyperaemia. The following year Hechter, Lev, and Soskin suggested that the effect of oestrogens on the uterus was twofold: (a) the specific oestrogenic action not depending on hyperaemia, and (b) an action secondary to the production of hyperaemia. The relative importance of these two effects was discussed in relation to the importance of hyperaemia in the production of periodic menstrual bleeding in the human subject. Since uterine hyperaemia is, presumably, also conditioned by the parasympathetic nervous system, certain cases of amenorrhoea, it was argued, might be due to the influence on the parasympathetic of such factors as fear, emotion, and physical strain, rather than to endocrine deficiencies. In these cases there would be better results from pharmacological treatment than from endocrine.

Acetylcholine was considered unsuitable as a drug owing to its dangers, and a synthetic physostigmine-like compound, " prostigmine ", was suggested instead. Prostigmine was shown to be a safe drug when administered to pregnant women. Certain limitations were appreciated, in that it has no effect on amenorrhoea due to an early meno-

pause, endocrine dysfunction, or local pelvic changes. Prostigmine, 2 ml., was administered on each of three successive days to 200 patients suffering from amenorrhoea on 216 separate occasions, each of which was counted separately in the statistical analysis. The injection of prostigmine was followed by the onset of menstrual flow in 77 of the 216 administrations. In 68 of these (88 per cent) bleeding occurred either during the course of the injections, or within 3 days afterwards—that is to say, within 5 days of the first injection. In the remaining 9 bleeding occurred after an interval of up to 15 days and had, therefore, a doubtful relationship to the injections. None of the individuals was pregnant. The length of previous amenorrhoea (up to 45 days) bore no relation to the length of time before the response. In the remaining 138 cases no menstruation followed, and of these, 137 patients were subsequently found to have been pregnant. The remaining patient (false positive) was undergoing an early menopause. In these patients no untoward symptoms developed as a result of the injections. A direct comparison between the value and accuracy of the Friedman test and of the prostigmine test in the diagnosis of pregnancy was not possible from the data obtained, as the Friedman test was performed at different times from the prostigmine test, and not on all the patients. In some cases, at least, the latter appeared to be more reliable.

D. M. Stern

99. The Problem of " Postmaturity "

By A. J. WRIGLEY. *Proc. R. Soc. Med.*, 39, 569–574, July 1946. 25 refs.

Wrigley points out that pregnancy ending later than the expected date of delivery is not associated significantly with the birth of overdeveloped children. The difficulties in labour sometimes ascribed to postmaturity would be more correctly attributed to the size of the baby, and a large child is as likely to be found at or even before the expected date of delivery. The form of management is deprecated which, with the intention of preventing dystocia due to so-called postmaturity, insists on induction of labour at any set time in relation to the calculated date. Attempts should be made to assess accurately the size of the baby at each examination during the later weeks of pregnancy, and if the baby is thought to be large it may be

expedient to induce labour. The thoughtless use of medical induction of labour in such cases as a test of maturity is unwise; medical induction should be reserved only for cases where it is necessary, and the obstetrician is prepared to attempt a surgical induction within a few days if drugs fail.

Wrigley notes the difficulties in assessing the bulk of the foetus by clinical or radiological means. He suggests that a large foetus with strong rigid limbs, filling a uterus which contains relatively little liquor amnii, is generally overdeveloped.

W. I. C. Morris

100. A Thickness Technique in Radiographic Examinations of the Abdomen and Pelvis.

By G. D. STEVEN. *Brit. J. Radiol.*, 20, 58–60. February 1947. 1 fig.

101. Some Applications of Prenatal Nutrition to Infant Development.

By A. ST. G. HUGGETT. *Brit. med. Bull.*, 4, 196–204, 1946. 5 figs., 60 refs.

There are two main prenatal factors—the genetic and the nutritional—which affect the chances of survival and the health of the infant. This paper gives a review of the work done on the nutritional factors. The curve of growth *in utero* becomes very steep in the last 3 months of pregnancy, more than two-thirds of the birth weight being acquired in the last 8 weeks; three-quarters of this is water. Depletion of the maternal food supplies lowers the birth weight. It has been demonstrated that the diet in the last 8 weeks of pregnancy affects not only growth of the foetus but also that of the mammary gland and the eventual milk yield. A decrease in birth weights has been observed in occupied European countries, together with an increase in neonatal mortality. In Britain diet restrictions due to the war have not been proved to lower the birth weight (Huggett, *Proc. Nutrit. Soc.*, 1944, 2, 20). Hammond showed that the ratio of the weight of single lambs to the weight of individual twin lambs is proportional to the degree of nutritive impairment. Applying this ratio to the birth weights of London during 1938–1939 and 1941–1942, there is actually an indication of improved health and chance of survival.

The foetus can, to some extent, maintain its body weight when the maternal food is in short supply. Hammond (*Proc. Nutrit. Soc.* 1944, 2, 8) proposed

the theory of partition of nutrients to explain this. This theory states that in early life the higher total metabolic rate of foetal tissues enables the foetus to compete successfully with the lower metabolic rate of the maternal tissues and in this way obtain its desired quota of nutriment. The placenta is also a competitor for nutriment, and in the human subject at full term is bears a ratio to the foetus of one-quarter to one-twelfth. Therefore, the larger the placenta the better the storage and diffusion capacity and so the greater chance of foetal survival.

The total iron present in the diet of the pregnant mother determines the severity and duration of the anaemia which occurs during the first year of life. The mother showing an active hypochromic anaemia usually has an infant with no anaemia at birth. Apparently the embryo with its higher metabolic rate has taken the available iron at the expense of the mother with her low metabolic rate. This is not a complete answer, as within the embryo the erythrocyte shows no iron deficiency at birth. Fullerton (*Arch. Dis. Childh.*, 1937, **12**, 91) regards the reserves of iron available to the erythrocytes as being in the blood itself apart from sources available in the food supplied in the postnatal period, and for this reason he emphasizes the importance of feeding iron to the infant, at the same time doubting the value of supplementary iron in the diet of the pregnant woman. The author considers that in view of the work of Strauss (*J. clin. Invest.*, 1933, **12**, 345) and Smallwood (*Brit. med. J.*, 1936, **2**, 573) it is doubtful whether Fullerton's conclusions are wholly correct. If calcium, phosphorus, and vitamin D are not supplied in the maternal diet in adequate amounts not only is the postnatal development of the infant affected but also a loss of calcium from the maternal tissues occurs, as the higher rate of metabolism of foetal bone growth *in utero* makes a priority demand on the nutrients required. The author concludes that the balanced diet in pregnancy is essential for foetal and infant health, quite apart from the obvious advantages conferred on the mother.

R. Winston Evans

102. **Maternal Diet, Infant Mortality, Breast Feeding, Child Health.**
By I. G. MACY. *Med. Wom. J.*, **53**, 21–26, October 1946. 9 refs.

ABNORMAL.

103. **Recurrent Eclampsia.** (Eclampsia de repetición ; notas de casuistica.)
By V. NOTARIO GARCIA and A. GARCIA HERNANDEZ. *Rev. esp. Obstet. Ginec.*, **5**, 92–99, August 1946. 21 refs.

Four cases of recurrent eclampsia are described. The incidence of eclampsia in these series was 1.4 per cent (25 cases in 1,727 pregnancies). The recurrent form occurred in 16 per cent of patients who had a previous history of eclampsia. Most authors confirm this increase in incidence. It is well known that eclampsia occurs mainly in primigravidae, and the relative rarity of recurrence is hard to explain. It is suggested that a process of iso-immunization takes place in eclamptic mothers, although it must be remembered that in many cases a woman who has once had eclampsia will receive prophylactic treatment in subsequent pregnancies and on this account may never pass the stage of pre-eclampsia. It is possible that in pre-eclampsia the motor cortex and the ganglia of the mesencephalon are in a state of excitability, and may be acted on by a variety of precipitating factors, any one of which may produce the convulsions of eclampsia. A review of the literature reveals no single specific agent. Certain factors in the cases described are considered in relation to eclampsia. Foetal factors include sex and number of foetuses, a higher proportion of male foetuses being noted in cases of eclampsia. In multiple pregnancy the incidence of eclampsia is greatly increased. Constitutional anomalies of familial distribution may be found in the mother, as well as vascular disorders, liver deficiency, or endocrine instability. The authors feel that eclampsia may arise from iso-immunization and that investigation should proceed along these lines.

[The suggestion in this article seem to be based on a very small number of cases.]

Josephine Barnes

104. **The Effect of Essential Hypertension on Pregnancy.**
By J. A. SHARKEY and C. B. HESS. *Amer. J. Obstet. Gynec.*, **52**, 672–676, October 1946. 6 refs.

The authors define essential hypertension as an elevation of blood-pressure to 140 mm. systolic and 90 mm. diastolic or more, existing for 2 days or longer without any signs or symptoms of renal

disease. The patients studied were 115 women out of a series of 3,000 patients delivered consecutively in the Hospital of the University of Pennsylvania.

Fifty-two of the 115 patients developed albuminuria of varying degrees. The retinal fundi of 33 patients were examined. Twenty-one were found to have early sclerotic changes with some spasm, 2 showed marked arteriosclerosis, and 10 were normal One patient had an abruptio placentae in the eighth month of pregnancy. Eight patients had a blood-pressure of at least 200/100 at some time during their pregnancies. In 4 of the latter the pregnancy was interrupted by either therapeautic abortion or hysterotomy; the remaining 4 were delivered of normal infants at term.

Of 2,885 pregnancies not associated with essential hypertension 737 (25 per cent) ended in abortion, premature birth, or neonatal death. Of 115 pregnancies in this series 20 (17 per cent) ended in this manner. Blood-pressure was normal in half of the 90 women who were examined 6 weeks after delivery. The authors compare their incidence of unsuccessful pregnancy with that obtained by Dieckmann (21 per cent) and by Browne and Dodds (36.5 per cent).

[It must be emphasized, however, that the latter are dealing with quite a different type of case from many of those included in the present series—that is, with cases of hypertension with or without renal involvement and existing *before* pregnancy, in other words, with chronic vascular hypertension. In the authors' series, no limit appears to be set to the time in pregnancy at which the hypertension first appears. The consequence of this is that many cases must be included in which hypertension appears for the first time late in pregnancy, and which would therefore be classified by other authors as cases of pre-eclamptic toxaemia. This applies to patients in whom the first rise in blood-pressure occurs after the twentieth week of pregnancy.]

F. J. Browne

105. **Protein Depletion in Pregnancy Toxemia.**
By H. SPITZER. *West. J. Surg.,* 54, 392–393, October 1946. 9 refs.

Altogether 101 quantitative determinations of total serum protein, albumin, and globulin were made in Curacao on 89 coloured people in the low-income group (Kjeldahl method of nitrogen estimation). Seventy-one patients came in for their first

antenatal examination round about the eighth month; 28 of these showed no oedema, and 43 had oedema. Thirty individuals, 18 non-pregnant women and 12 men, both groups without evidence of oedema, were used as controls. The results are shown in the table:

	Men	Non-pregnant women	Pregnant women without oedema	Pregnant women with oedema
AVERAGE VALUES				
Osmotic pressure (cm. water)	44.5	43.5	40.9	32.8
Total protein (g. per 100 ml. of blood) ...	7.9	7.7	7.3	6.5
Albumin (g. per 100 ml. of blood)	5.2	5.1	4.7	3.6
Globulin (g. per 100 ml. of blood)	2.6	2.6	2.5	2.9
MAXIMAL VALUES				
Osmotic pressure ...	50.3	54.2	54.5	47.4
Total protein	9.0	8.6	8.7	7.7
Albumin	6.1	6.0	7.7	5.8
Globulin	3.7	4.0	4.1	5.1
MINIMAL VALUES				
Osmotic pressure ...	38.0	35.5	30.9	16.0
Total protein ...	6.8	6.8	5.3	3.0
Albumin	4.2	4.3	3.2	2.1
Globulin	1.8	1.5	0.9	0.8

Osmotic pressure is associated with albumin and globulin only. The 4 different values for maxima and minima do not necessarily belong to a single case. There is a significant gradual decline in the level of the blood proteins in the order—males, non-pregnant women, gravidae without oedema, gravidae with pregnancy oedema. While in an average non-pregnant woman a reduction of the albumin level to 2.5 per cent and of the total protein to 5 per cent is supposed to be essential to cause oedema, it appears that higher protein levels are associated in pregnancy (albumin 3.6 per cent and total protein 6.5 per cent are average values in pregnancy oedema). The difference is explained by the increased venous pressure in pregnancy. There are cases of oedema produced by this factor alone. Oedema in pregnancy does not justify the conclusion that the blood proteins are reduced; therefore, it is essential in any such case to determine their levels. There is normally an increase in the total blood volume during the latter part of pregnancy. Some authors have claimed that the reduc-

tion of plasma protein is the result of dilution, overlooking the individual reduction of the albumin fraction. The maximal values found in the present observation suggest that pregnancy can take place without any reduction of the blood proteins, but the average values prove that such a reduction is very frequent.   *D. M. Stern*

106. Oedema of Vulva due to Toxaemia of Pregnancy.

By J. P. BUSH. *Brit. med. J.*, 2, 988, December 28, 1946. 1 fig.

The case reported is one of vulvar oedema so marked as to obstruct normal delivery. The patient, a young primigravida of 21 years, attended the antenatal clinic throughout her pregnancy. At the thirty-sixth week of pregnancy her blood-pressure was 150/95 mm. Hg. Two weeks later her blood-pressure was 150/105, and there was considerable albuminuria with gross oedema of legs, thighs, and abdomen. The patient was admitted to hospital, when it was found that there was also considerable oedema of the vulva. In spite of fluid restriction, a salt-free low-protein diet, and 3 mg. vitamin B$_1$ given thrice daily, the vulvar oedema became more marked; the urine contained 6 parts of albumin per 1,000 and the blood-pressure was 140/110. Urinary excretion was normal. Two days after admission to hospital the pregnancy was terminated by classical Caesarean section as the toxaemia was not responding to treatment and the vulvar oedema was so gross as to obstruct normal delivery. Catheterization was not possible. At operation the peritoneal cavity contained 1 to 1½ pints (568 to 852 ml.) of pale yellow fluid. A normal male child weighing 6 pounds 1 ounce (2.75 kg.) was delivered. After delivery the blood-pressure quickly returned to normal. The albuminuria cleared up after 10 days, and the oedema subsided within 10 to 14 days.
                    T. N. MacGregor

See also No. 91

107. Discussion on Placenta Prævia.

By C. H. G. MACAFEE, L. PHILLIPS, J. BARNES, J. YOUNG, J. M. MUNRO KERR, A. W. PURDIE, R. C. THOMAS, J. STALLWORTHY, and F. J. BROWNE. *Proc. R. Soc. Med.*, 39, 551–558, July 1946.

Macafee describes the policy of the Royal Maternity Hospital, Belfast, where in 1937 it was decided to allocate the 3 common emergencies to 3 different members of the visiting staff, all cases of antepartum haemorrhage being allocated to the author. He presents the results of 191 cases showing a single maternal death (0.52 per cent) and a total of 42 foetal fatalities (an uncorrected fatality rate of 22 per cent). The main object of treatment has been to reduce foetal mortality without unfavourably affecting the maternal condition. Since the most important cause of foetal death in placenta praevia is prematurity, this object is best attained by expectant treatment, as in this series.

Macafee advises the discontinuance of the terms " lateral ", " marginal ", and " central ", with the substitution of Browne's classification into 4 " types " or " degrees " (F. J. Browne, *Antenatal and Postnatal Care*, London, 1946, p. 240). He points out the importance of the site of placental insertion of the umbilical cord in relation to foetal death. If the cord insertion is near the area where separation takes place, the foetus frequently dies when infarction of the separated placenta occurs. Apart from speculum examination, which should be carried out after the first bleeding, vaginal examination should be delayed until the end of the period of expectant treatment, and should then be carried out in the operating theatre with everything in readiness for Caesarean section, which is called for in Type III and Type IV placenta praevia (where the placenta covers the internal os) and also in cases where a placenta on the posterior wall reaches the internal os (that is, a Type II placenta praevia situated posteriorly; the dangerous nature of this type was stressed in discussion by J. Stallworthy). In other types of placenta praevia artificial rupture of the membranes will generally suffice.

The paper is discussed, with presentation of comparative statistics, by the other obstetricians named in the title.   *W. I. C. Morris*

108. Causes of Prematurity. VIII. Influence of Infections, Chronic Disorders and Accidents on the Incidence of Prematurity.

By E. W. BROWN, R. A. LYON, *and* N. A. ANDERSON. *Amer. J. Dis. Child.*, 72, 189–201, August 1946. 3 refs.

The same authors have previously reported the results of their investigations of the relationship of maternal syphilis, toxaemia, and uterine bleeding

to premature onset of labour. The present analysis is carried out along similar lines, but the incidence of infections and chronic disorders in the series of 13,525 mothers was too low to permit statistical analysis. Of the entire series of 682 mothers who gave birth to premature infants only 8 per cent had acute infections, 7 per cent had chronic disorders, and fewer still had accidents and other complications. As in previous reports, the standard of prematurity was taken as a birth weight of less than 5 pounds 8 ounces (2.5 kg.) for white babies, and less than 5 pounds 3 ounces (2.25 kg.) for negro babies, these weights corresponding to comparable stages of development. With this adjustment the figures for white and negro mothers do not differ significantly.

Premature delivery occurred in 14 per cent of women who had acute infections during pregnancy (including tuberculosis, pneumonia, influenza, pyelitis, otitis, and acute gonorrhoea), in 10 per cent of women with chronic disorders (including heart disease, nephritis, and diabetes), and 'in approximately 10 per cent of those suffering accidents during pregnancy (including surgical operations) and complications of labour (such as abnormal presentations and premature rupture of membranes). All these conditions appeared to exert a slight influence in raising the incidence of prematurity above the figure of 5.5 per cent for women who had entirely normal pregnancies. The influence of chronic infections is not so clearly demonstrated in this analysis of single births as when complete family histories were examined, in which case the incidence of stillbirth was found to be distinctly high.   *M. Baber*

109. **Repeated Abortions, Miscarriages and Stillbirths. Value of Antisyphilitic Treatment.**
By R. G. CROSS. *Lancet*, 2, 754–755, November 23, 1946. 1 ref.

The incidence of repeated abortions, miscarriages, and stillbirths is low, being less than 0.4 per cent of 15,780 deliveries at the Rotunda Hospital in 3 years. It was decided that, since good results were obtained in treating these conditions in syphilitic mothers, it would be worth giving anti-syphilitic treatment to patients with no history of syphilis and in whom the Wassermann reaction was negative, but who had a history of repeated abortions, miscarriages or stillbirths. The results

in 54 cases are given, and it is claimed that a marked improvement resulted. These 54 patients had previously had 55 live babies out of a total of 249 pregnancies, but after treatment they had 49 live babies out of 54 pregnancies. It is suggested that syphilis might have been present in some of the fathers of these babies.

[This work requires criticism on several grounds. First, the statistical data seem unreliable. Other factors than the giving of anti-syphilitic treatment may have been involved. For example, vitamin E and calcium were given. These were not cases of true habitual abortion since many already had living children, and 1 patient in the series had no less than 6 previous live births. If syphilis was suspected in the fathers of these babies why were tests not carried out on them to exclude this? Good results have been claimed in cases of habitual abortion with diverse methods, and the work of Malpas and others has shown that detailed analysis of a large series of cases is needed to prove the value of any one method of treatment. Many of the patients in this series were not seen until late in pregnancy, 11 out of the 54 not before the thirtieth week. Finally, anti-syphilitic treatment is not without inherent danger and seems to have been unjustified in these cases.]
                              Josephine Barnes

110. **Placental Changes in the Rabbit in Abortion Produced by Oestrogens.** (Alteraciones placentarias de la coneja en el aborto provocado por estrogenos.)
By R. SAMMARTINO and O. BLANCHARD. *Obstet. Ginec. latino-amer.*, 4, 533–549, July 31, 1946. 8 figs., 53 refs.

Many references can be found in medical literature to the effect of large doses of oestrogens on the pregnant rabbit, in which death and expulsion of the foetuses result. This has been attributed by various authors mainly to the primary effect on the corpus luteum. No studies of the histological lesion in the placenta are available, and these form the subject of the present article.

The material chosen consisted of rabbits in the second half of pregnancy (fifteenth to thirteenth day). It was found that a single injection of 0.25 mg. of oestradiol benzoate or 0.125 mg. of stilboestrol dipropionate would constantly produce abortion in rabbits 15, 20, 21, and 22 days pregnant. Expulsion of the foetuses occurred, 5, 6, or 7 days

after injection. Three series were studied, one series being a control, one being treated with stilboestrol dipropionate and killed at intervals varying between 4 and 65 hours after injection, and a third being treated with oestradiol benzoate and killed 8 to 144 hours after injection.

A description of the normal placenta in the rabbit is given. In animals injected with oestrogen the first change observed was vasoconstriction in the maternal uterine blood vessels. Later, inhibition of growth in the foetal ectoderm was observed, and by the twenty-fourth hour these changes, together with pyknosis in the nuclei of the foetal cells, were well marked. By the fortieth hour haematomata of the maternal blood appeared in the placenta. Sixty hours later the ovum was being detached and necrosis in the placental tissues was well marked. The authors think that oestrogens act directly on the foetal ectoderm. No apparent involutionary lesions were noted in the corpora lutea.

[It has long been known that oestrogens will procure abortion in the pregnant rabbit, though various theories have been put forward. It is good to have a satisfactory explanation of the mode of action of oestrogens and to find that they act apparently on the foetal tissues, or possibly through vasoconstriction in the uterus. In connexion with endocrinology these observations illustrate the fallacy of arguing from one animal to another. The results obtained in rabbits do not, in general, appear to apply with regard to the human uterus and endocrine system.]

Josephine Barnes

111. Induced Abortion on Eugenic Indications.
By T. KEMP. *Acta psychiat. Kbh.*, 21, 417–427, 1946. 4 refs.

112. Hydramnios.
By L. C. RIVETT. *Amer. J. Obstet. Gynec.*, 52, 890–893, December 1946. 4 refs.

113. Endometriosis in Association with Pregnancy.
By F. R. LOCK and R. T. MYERS. *Amer. J. Obstet. Gynec.*, 52, 556–563, October 1946. 37 refs.

There has been an apparent increase in the incidence of pelvic endometriosis in recent years. A full review and summary is given of a paper by R. B. Scott (*Amer. J. Obstet. Gynec*, 1944, 47, 608–632). Most of the present paper is concerned with the results given by Scott; it reiterates the conclusion that pelvic endometriosis is not a particularly dangerous complication of pregnancy and that treatment should be conservative in young patients with endometriosis or adenomyoma. Details are given of 2 personal cases where successful pregnancy followed conservative treatment for severe endometriosis.

[Apart from 2 extremely interesting case reports, in themselves a valuable addition to the literature, this paper contains little that is original.]

Josephine Barnes

114. Cancer of the Breast and Pregnancy. (Bröstkräfta och havandeskap.)
By K. KETTUNEN. *Nord. Med.*, 31, 1747–1750, August 9, 1946. 17 refs.

Breast cancer is uncommon during pregnancy. The majority of cases occur in elderly multiparae. Pregnancy aggravates the condition, whether it has arisen before or during the event. This aggravation is due to the increased amount of oestrogenic hormones in the blood of the pregnant woman. Breast cancer arising during lactation is not so malignant, the amount of oestrogenic hormone being then lower. Where a case is diagnosed during pregnancy the latter should be interrupted before radical mastectomy is performed. Sterilization of all women suffering from breast cancer would be beneficial.—[From the author's summary.]

115. Masculinization and Pregnancy: A Case Report.
By R. W. BAIRD and E. B. ASTWOOD. *Bull. New Engl. med. Center*, 8, 234–239, October 1946. 3 figs.

116. Retroperitoneal Hemorrhage Complicating Pregnancy. Report of a Case.
By C. T. O'CONNOR and J. J. BRADLEY. *New Engl. J. Med.*, 235, 648–650, October 31, 1946. 6 refs.

The authors describe a case of retroperitoneal haemorrhage occurring in pregnancy. The patient, aged 38, had always been healthy and had one child 11 years old; the confinement had been normal. She was quite well during the antenatal period and had been carefully examined from time to time; when she was a week overdue she was admitted to hospital because she had developed pain in the left lower abdomen. Her general condition was quite good and the pain not severe, but

on vaginal examination a large mass was felt in the pelvis behind and to the left of the cervix. A diagnosis of fibroid likely to obstruct labour was made, and a Caesarean section was performed. At operation a large retroperitoneal haematoma was found in the true pelvis spreading up to the meso-colon. Convalesence was uneventful, but when the patient was examined 6 months later some thickening was still felt in the region of the haematoma and she had some pain. The authors refer to other cases of retroperitoneal haemorrhage reported in the literature. All of these were fatal and were initially associated with- severe shock; the main haemorrhage was in the upper abdomen and especially in the region of the left kidney. The authors' own case thus differs greatly from the reported ones.

L. W. Lauste

117. Terminal Ileitis with Obstruction and Abscess Complicating Pregnancy.

By W. W. BABSON. *New Engl. J. Med.,* 235, 544–547, October 10, 1946. 10 refs.

A case of intestinal obstruction due to regional ileitis at the seventh month of pregnancy is described. Since the start of pregnancy the patient, a primipara, aged 25, had noted increasing constipation and some tenesmus, now and again with diarrhoea. Two months before admission there was sudden severe pain in the right lower quadrant of the abdomen. This gradually passed off and was followed by repeated attacks of milder abdominal pain and bouts of vomiting with a gradual worsening of the general condition. On admission to hospital the patient was gravely ill. A tender mass in the right side of the abdomen had pushed the uterus across to the left. The uterus was contracting strongly at intervals and the foetus was living. A barium enema revealed narrowing and fixation of the terminal ileum. The diagnosis of probable terminal ileitis with obstruction was made. The onset of severe pain 2 months previously was regarded as representing a perforation. A Miller-Abbott tube was passed and the following day operation was undertaken with continuous spinal analgesia. A large inflammatory mass was found involving the terminal 75 cm. of the ileum; the appearances were typical of cicatrizing ileitis with fistula and abscess. The ileum was divided well above the lesion, the distal end was closed and

invaginated, and the proximal end was anasto-mosed to the transverse colon in an end-to-side manner. Recovery was complicated by jaundice, believed to be due to toxic hepatitis. Serum pro-tein fell to 4.3 g. per 100 ml. in spite of repeated blood transfusion and the administration of intra-venous amino acids and glucose. On the tenth day after operation the patient went into active labour and a living infant was delivered weighing 3 pounds (1.35 kg.). The baby lived only a few hours. On the fourteenth day the mother complained of severe pain in the lower abdomen and there were signs of spreading peritonitis. Further transfusions and penicillin were given and localization in the pelvis began to take place. Five days later a pelvic abscess was evacuated through the vagina. From this point on improvement was rapid. A year later she was reported as remaining well.

The author stresses the importance of paying full attention to symptoms of abdominal pain in pregnancy. This patient had, in fact, been admitted to 2 different hospitals during the 2 months of abdominal pain and vomiting which preceded her operation. On the first occasion she had been discharged with a diagnosis of gastro-enteritis, and on the second no diagnosis was reached and she was stated to present no evidence of disease. He notes how difficult the management of abdominal surgical conditions in pregnancy may be, and is guided by the rules that if delay is safe postponement of operation is advisable, but if operation is necessary the pregnancy must be disregarded. He summarizes the treatment of ileitis as follows. Acute non-obstructive lesions in the early stages should not be disturbed, since the aetiology is unknown and recurrence is frequent. Surgery is indicated for patients with obstruction, fistula, or abscess or for those who are unable to maintain weight and strength under adequate medical management. As to the type of surgery, he notes that excellent results have been reported both with the exclusion operation and with resection. He points out that in the case described there was no choice of the type of surgical procedure, fixation and inflammation completely ruled out resection. The result of exclusion in this case was so good that further surgery was not considered advisable.

H. J. Croot

118. Acute Lymphatic Leukemia and Pregnancy.
By J. R. ALMKLOV and A. HATOFF. *Amer. J. Dis. Child.*, 72, 202–206, August 1946. 10 refs.

A case of acute lymphatic leukaemia in a pregnant woman is recorded. The patient, aged 26, complained of febrile symptoms about the twenty-eighth week of her second pregnancy. Examination showed generalized enlargement of the lymph nodes and spleno-hepatomegaly. The peripheral blood contained 170,000 leucocytes per c.mm. of which 95 per cent were lymphocytes. A haemorrhagic state developed, and she died after 3 weeks' illness. Postmortem, the usual features of lymphatic leukaemia were found, and the uterus contained a 7-months foetus, with talipes and spina bifida. The authors have found records of leukaemia associated with pregnancy in 84 instances. The placental barrier resists the passage of leukaemic cells, and there is no recorded example of a leukaemic mother bearing a leukaemic child. They recommend that leukaemia in pregnancy should be treated in the conventional manner, but that resort be made to Caesarean section if the mother's health is failing rapidly.

R. Bodley Scott

119. Funicular Myelosis in Pregnancy. (Funikuläre Myelose als Schwangerschaftserkrankung.)
By J. AIGINGER. *Wien. klin. Wschr.*, 58, 688, November 15, 1946.

120. Funicular Myelosis in Pregnancy. (Funikuläre Myelose als Schwangerschaftserkrankung.)
By A. STINGL. *Wien. klin. Wschr.*, 58, 688–689, November 15, 1946. 3 refs.

121. Strangulated Umbilical Hernia Complicating Pregnancy.
By W. C. NEWMAN. *Manitoba med. Rev.*, 27, January 19, 1947.

122. The Treatment with Massive Arsenotherapy of Early Syphilis Complicated by Pregnancy.
By A. C. CURTIS and G. MORROW. *Amer. J. Obstet. Gynec.*, 52, 284–290, August 1946. 16 refs.

It is claimed in this paper, published by the Department of Dermatology and Syphilology, University of Michigan Medical School, that massive arsenical therapy offers a rapid and efficient method of treating syphilis in pregnancy. The results of Jeans (*Amer. J. Syph., Gon. Vener. Dis.*, 1919, 3, 114) and of Marshall (*J. Amer. med. Ass.*, 1934, 102, 503) are quoted to show the high incidence of stillbirth, abortion, and infant mortality when pregnant women with latent syphilis are untreated. The results of Marshall, McKelvey, and Turner (*J. Amer. med. Ass.*, 1934, 102, 503) and others are quoted to show that the foetal prognosis is proportional to the adequacy of antenatal anti-syphilitic treatment.

The good results of Sudusk and Shaffer (*Yale J. Biol. Med.*, 1942, 14, 34), Rattner (*Amer. J. Obstet. Gynec.*, 1943, 46, 255), and others with massive arsenotherapy by the 5-day drip method are recorded. The authors give their own results in 30 cases treated by the total injection of 1,200 mg. of mapharside with 260 mg. of bismuth. They then describe the treatment of 10 cases by a modified technique in which a total of 1,080 mg. of mapharside in 5 per cent glucose was given intravenously by daily injections with the associated administration of 4 doses of 130 mg. of bismuth subsalicylate in oil intramuscularly. Liver and renal function were tested and a blood count was made before treatment was begun. Neither abortions nor stillbirths occurred in this series. The fallacies of the testing of cord blood, of the Wassermann test, and of examination of the placenta are emphasized. The value of dark-ground examination of serum from the umbilical vein or infant's skin is also emphasized.

J. Stallworthy

123. Syphilis in Pregnancy. (Sifilis en el embarazo.)
By J. D. MESA RAMOS. *Bol. Soc. cubana Derm., Sif.*, 3, 97–119, September 1946. 12 refs.

124. Hysterosalpingography in Extra-uterine Pregnancy. (Hysterosalpingografisk undersögelse ved extrauteringraviditeten.)
By B. NIELSEN. *Nord. Med.*, 32, 2337, October 11, 1946.

This preliminary assessment of the value of hysterosalpingography in the diagnosis of extra-uterine pregnancy is based on 25 cases. Of these, 12 were found to have extra-uterine pregnancy, and in 6 of these hysterosalpingography had given a characteristic picture, in 5 a doubtful picture, and in 1 case there was no air entry into the tube. Of the remaining 13 patients hysterosalpingography excluded extra-uterine pregnancy in 8 cases by showing normal patent Fallopian tubes. Whether this method of investigation will find a place in diagnosis depends on whether it is accurate, whether other methods available are sufficient to

establish a diagnosis, and whether any special risk or inconvenience is attached to the investigation itself. Apart from the slight risk of lighting up infection which always attends this method of investigation there is no danger in its use in extra-uterine pregnancy. More details of its accuracy will be given in a later communication, but up to the present, though there is a group of cases where its results are doubtful, it has been found to give characteristic pictures which either make the diagnosis of extra-uterine pregnancy or definitely exclude it. In this connexion the possibility of false findings in cases of ovarian, intra-abdominal, or coincident tubal and uterine pregnancy must be remembered. The investigation is contra-indicated in the presence of acute infection. Its importance lies in the fact that it can exclude intra-uterine pregnancy and thus prevent unnecessary laparotomy.

J. W. S. Lindahl

125. **Bilateral Simultaneous Tubal Pregnancy.**
By J. F. MacDonald and V. E. Masters. *Amer. J. Obstet. Gynec.*, 52, 850–853. November 1946. 1 fig.

126. **Foetal Bones in Urinary Bladder. Unusual Termination to Ectopic Pregnancy.**
By H. W. Forshaw. *Lancet* 2, 716, November 16, 1946.

In the case here reported the patient, an African woman aged 38, married 15 years, with no children, attended an out-patient clinic in Nigeria, bringing with her a number of small bones which she stated she had passed in her urine on 3 occasions in the preceding 3 months. There was no history of haematuria, and no pain except when the bones were passed. The bones had the appearance of small vertebrae. A significant point in her past history was that 9 years previously she had become pregnant and had gone to full term when she was seized with severe abdominal pain accompanied by slight vaginal haemorrhage. The pain and haemorrhage lasted for less than a day and the swelling of the abdomen gradually subsided in 3 months. The bladder was opened and a mass of foetal bone was removed, among which part of a mandible, ribs, and skull bones could be identified. In view of the history and clinical findings the condition is considered to be the result of an old ruptured ectopic pregnancy which had ulcerated through into the bladder.

[This explanation, though no doubt correct, may perhaps be amplified. The history strongly suggests that pregnancy had in fact continued to term. The death of the foetus within the abdomen would be followed by the gradual absorption of everything but its bones.]

T. C. Clare

LABOUR

127. **Early Signs of Difficulty in Labour.**
By G. F. Abercrombie. *Med. Press*, 216, 420–423, December 4, 1946.

128. **The Use of Posterior Pituitary Extract in the First and Second Stages of Labour.**
By J. S. Brewer, G. M. Cooper, E. W. Franklin, J. S. Hunt, T. L. Lee, I. Procter, R. A. Ross, R. A. White and F. R. Lock. *North Carolina med. J.*, 7, 568–569, October 1946. 7 refs.

The authors of this article are members of a Maternal Welfare Committee. After a brief historical review of the use of pituitrin in obstetrics, it is pointed out that the difficulty in its use arises from the large number of factors tending to produce variations in response of the uterus to the drug. Such factors are irritability of the uterus, rate of absorption of the drug, parity, duration of pregnancy, degree of distension of the uterine wall, and others less tangible. The great danger of unusual response is illustrated by the report of uterine rupture after a 2-minim dose. Dangers to the foetus arise: (a) from slowing of the blood flow in the utero-placental sinuses with abnormally violent or prolonged contractions and (b) from the fact the foetal head must bear the brunt of increased intra-uterine pressure, after the membranes have ruptured. A first injection of ½ minim of pituitary extract given accurately from a tuberculin syringe is recommended. Further doses, if required, may be increased by ½ minim a time and given at not less than 30 minute intervals. Ether inhalation should be available in case uterine tetany occurs. The following conditions must obtain: (1) true labour with contractions much less than average in strength and frequency must be present; (2) the uterine muscle must be inert, as seen by its denting on pressure with one finger at the height of a pain; (3) there must be no mechanical obstruction to delivery, the position and presentation must be known, and the presenting head must be engaged;

(4) either the membranes should be intact, or, if not, the cervix should be fully dilated and the head on the perineum; (5) at least 5 cm. dilatation of the cervix must be present; (6) the condition of the foetus must be good; (7) the obstetrician must not leave his patient. Contra-indications to the use of the drug are normal contractions,. placenta praevia, abnormal presentations, and abnormally large baby, hydramnios, or twins. [N.B. Doses are not given in units in the article.]

S. S. B. Gilder

129. **Bracht's Method of Breech Delivery.** (Over de methode van Bracht bij stuitligging.)
By P. E. REYNDERS. *Belg. Tijdschr. Geneesk.,* **2**, 534–548, September 1946. 1 fig., 24 refs.

The author points out the still considerable child mortality (10 to 15 per cent) in spontaneous breech presentations delivered by the commonly used methods. He agrees with Schwarz (personal communication, 1945) that this mortality is mainly due to traumatic injuries of the abdominal viscera and to cerebral haemorrhages. He also stresses the findings of Brander (*Mschr. Geburtsh. Gynäk.,* 1937, **105**, 205) that there are twice as many mentally deficient children among those born by breech as among those born by vertex presentation (*Kongresbericht, International Kongres voor Verloskunde en Gynaecologie, Amsterdam,* 1938, **2**, 5, 93). Bracht has evolved a technique of delivery with which the margin of safety to the child and the mother is considerably increased. This technique is based on his observation that after the descent of the breech during a spontaneous delivery the back of the child rotates towards the mother's symphysis pubis, the shoulders and the head emerging in the transverse position and not in the antero-posterior, as commonly believed. Ruge claims that this is not the rule, there being individual variations, but Teufelmayer confirms Bracht's observation in many cases, while in other instances he has seen only the beginning of an unachieved rotation of the back. Bracht awaits the spontaneous descent of the breech and intervenes only when the inferior angle of the scapula has appeared. He then grips the child's body with both hands, the fingers of each hand on the back of the pelvis and the thumbs pressing the thighs flexed on the abdomen. The body thus held is rotated round the mother's symphysis until the child's back lands on the mother's abdomen. The shoulders emerge laterally, followed by the chin, nose, etc., sweeping the perineal floor. While this rotation is performed an assistant presses the head from above the symphysis towards the pelvic cavity. The whole manoeuvre takes only 3 minutes.

Bracht claims that mortality was nil in his 206 cases. With other workers mortality was 0 to 2.3 per cent; and their failures averaged 15 per cent, these being due to narrowed pelvis, extended arms, incomplete dilatation of the cervix. In such cases classical methods were adopted, only a negligible time being lost in attempting to apply Bracht's technique.

Reynders used Bracht's technique in 61 cases. There were 8 failures. Of the remaining 53, 4 children died in the first week from: polycystic kidneys (1), prematurity (weight 1,400 g. and 1,230 g.) (2) and cerebral haemorrhage (1). Only the last death could be ascribed to the technique. Among the 8 failures there were 2 deaths from cerebral haemorrhage; in both cases the arms were extended. Bracht's technique was also tried unsuccessfully in 3 cases of artificial extraction of the breech.

A. Lilker

130. **Breech Presentation and its Treatment.** (Die Beckenendlage und ihre Behandlung.)
By J. WEGLEITER. *Wien. klin. Wschr.,* **58**, 629–631, October 25, 1946.

131. **Manual Removal of the Placenta; a Benign Procedure.**
By C. W. SEWALL and D. COULTON. *Amer. J. Obstet. Gynec.,* **52**, 564–573, October 1946. 13 refs.

The authors do not believe that manual removal of the placenta is as dangerous a procedure as was formerly thought. They report the results in 45 cases in which the chief indications were blood loss, retention of the placenta, and advisability of exploring the uterus. They believe that the procedure should be carried out early to anticipate the onset of shock. The technique described differs little from that followed in most hospitals. Uterine packing is employed when necessary and ergotamine tartrate is administered as a routine after removal of the placenta. Transfusion or intravenous infusions are given when required.

The results show no mortality and a morbidity

of only 2.2 per cent. Records of 5 cases are given. Routine chemotherapy was employed in about half the cases, but the tendency was not to give it unless there was definite evidence of infection. It is concluded that manual removal is a relatively benign procedure if the patient is in good condition. A plea is made for a less rigid interpretation of the indications for manual removal and for earlier operation.

[This is a short series of cases, but there must be general agreement with the conclusions that manual removal performed early while the condition of the patient is good is preferable to repetition of Crédé's manoeuvre, or to waiting until shock has appeared.]

Josephine Barnes

132. Present Status of Transfusion of whole Blood and its Derivatives in Obstetrics and Gynecology.
By L. N. TISDALL. *Amer. J. Obstet. Gynec.*, 52, 788–793, November 1946. 11 refs.

ANAESTHETICS, ANALGESICS

133. Spinal Anesthesia—The Protector of the Baby in Cesarean Sections.
By K. M. HEARD. *Curr. Res. Anesth.* 25, 191–199, Sept.–Oct., 1946. 4 refs.

The baby born after administration of inhalation anaesthesia to the mother does not show the same spontaneous respiration or give the same lung-expanding cry as the baby delivered with other methods. It is not sufficiently appreciated that it is impossible to bring relief to the mother by sedatives or by inhalation anaesthetics without affecting the baby. The present investigation was designed to inquire into the effect on the infant and the mother of: (a) nitrous oxide or cyclopropane, (b) ether, and (c) spinal analgesia used for delivery by Caesarean section. The results of 360 Caesarean sections collected over 11 years are analyzed. Gas (nitrous oxide or cyclopropane) was given to 102 cases, ether to 73 cases, and spinal analgesia to 185. The patients anaesthetized by each of these three methods were divided into four groups: (a) normal mothers and normal babies, 202; (b) abnormal mothers (with toxaemia, cardiac decompensation, respiratory infection, metabolic dysfunction, and other affections) and normal babies, 90; (c) normal mothers and abnormal babies (with prematurity,

heart disease, prolapsed cord, or developmental abnormalities), 16; and (d) abnormal mothers and abnormal babies. Of the 202 babies in group (a) 20 per cent required resuscitation after gas, 18 per cent after ether, and 1 per cent after spinal analgesia. Of the 90 babies in group (b) resuscitation was needed for 20 per cent after gas, 6 per cent after ether, and 2 per cent after spinal analgesia. Of the 16 babies in group (c) 25 per cent needed resuscitation after gas, 85 per cent after ether, and 20 per cent after spinal analgesia. Of the 52 babies in group (d) 41 per cent required resuscitation after gas, 78 per cent after ether, and 27 per cent after spinal analgesia. [Though these figures are suggestive, the sub-groups are in most cases too small for them to be statistically significant.]

It is evident from these figures that spinal analgesia is the least harmful to the baby, but before reaching a conclusion as to its value its effect on the mother must also be considered. Moderate or severe surgical shock occurred in 18 per cent of the mothers given gas, in 9 per cent of those given ether, and in 15 per cent of those given spinal analgesics. Post-operative respiratory complications occurred in 8 per cent of the mothers receiving gas, in 12 per cent of those receiving ether, and in 10 per cent of those receiving spinal analgesics. Various techniques for spinal analgesia were used. In the one recommended as little pre-operative sedative was given as possible; ephedrine 30 mg. was administered with neosynephrine 0.2 ml. 10 minutes before lumbar puncture; 120 to 150 mg. of procaine crystals dissolved in 4 ml. spinal fluid was injected intrathecally slowly and without barbotage. An operating position with head lowered not more than 5 degrees was adopted, a change being made to the Trendelenburg position, if necessary, after 10 minutes, but only if intercostal movement was seen to be present. Blood pressure was supported throughout by pressor drugs or intravenous infusions.

Ronald Woolmer

134. Spinal Anesthesia in Vaginal Deliveries. Report of One Thousand Inductions.
By E. W. CARTWRIGHT and W. C. ROGERS. *West J. Surg.* 54, 346–351, Sept., 1946. 35 refs.

This paper is an attempt to establish, by statistics based on 1,000 cases, the authors' belief that spinal analgesia, properly used, is the safest and most effective of all methods known to-day

for the relief of pain in the latter part of labour, and for delivery and repair. They elaborate and emphasize the qualifying phrase " properly used ", defining it as the employment of a scrupulously careful technique by an expert. The disappointment that followed the first enthusiasm at August Bier's introduction of it in 1899 they attribute chiefly to " misuse amounting to incompetence and bungling ".. They criticize also, as misleading and chaotic, the mass of figures, covering a period of 40 years, on which the condemnation was based.

In their series of 1,000 cases the spinal analgesic was given when it appeared that delivery would occur within 1 or 2 hours, the time therefore depending on the frequency and strength of the pains. Generally primiparae were anaesthetized with the cervix 8 to 9 cm. dilated; multiparae with a dilatation of 6 to 7 cm. " Seconal ", often combined with " demerol " (pethidine), was given as a routine earlier in labour. Spinal analgesia was induced with the patient in the left lateral position, the spine being well flexed and the shoulders perpendicular to the table, the head of which was raised 1 to 2 in. (2.5 to 5 cm.). The injection was made through the lumbo-sacral interspace with a 20 to 22 gauge needle; occasionally the space above had to be used. The anaesthetic agent they are using at present is 10 mg. of pontocaine (amethocaine) in 2 ml. of 10 per cent glucose solution, though in the series here reported a variety of agents was used: procaine alone, in doses of from 50 to 100 mg.; pontocaine alone, up to 10 mg.; a combination of procaine, 50 mg., with pontocaine, 5 to 8 mg.; and sometimes " nupercaine " (cinchocaine) in 10-mg. doses. All drugs used were dissolved in 2 or 3 ml. of spinal fluid. Blood pressure, respiration, and pulse were checked every 15 minutes, and ephedrine was given if there was a marked drop in blood pressure. This, however, was rare, the great majority of patients not experiencing any significant fall. If the skin anaesthesia is kept down to, or below, the level of the umbilicus, a marked drop does not occur. The following are considered to be contra-indications; spinal deformities and spinal cord lesions; emotional conditions, such as fear; a blood pressure below 100 mm. systolic; skin infection; and haemorrhage. There was no maternal mortality nor mishap of any kind, and unpleasant reactions were few and mild.

T. C. Clare

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135. **A Report of 100 Cases of Trilene Analgesia in Labour.**

By A. P. BARRY and D. O'CONNOR. *J. med. Ass. Eire,* 19, 188-189, Dec., 1946. 2 refs.

In the last 2 years there has been increasing interest in the use of trichlorethylene (" trilene ") as a self-administered analgesic in labour. Trilene is a blue volatile liquid with a rather pleasant odour, which can be used as an analgesic and an anaesthetic. (Trichlorethylene is colourless. The commercial product, trilene, is artificially coloured. Its volatility is low.) It can be conveniently administered by Freedman's inhaler. This paper is an analysis of its use at the National Maternity Hospital, Dublin, in 100 cases. There was only 1 case of cardiovascular disturbance (with a rise in maternal, and a fall in foetal, heart rate) though the group included hypertensive and toxaemic cases. No respiratory disturbances were noted. There was no evidence of renal damage in the normal cases, and no deterioration of the renal condition in the 19 cases of toxaemia included in the group. No nerve palsies were observed.

Administration was begun in primigravidae towards the end of the first stage, and in multigravidae as soon as they were having good pains every 5 minutes. Labour was prolonged in 4 cases, quickened in 29, and unaltered in 65. The administration was stopped in 1 case because of hysteria, and in 1 because of tachycardia. Forceps were used (under ether) in 5 primigravidae because of failure of the head to advance; the failure may have been attributable to trilene in one of these cases. Trilene analgesia for perineal repair was effective in 20 out of 24 cases. In no case was the third stage prolonged. Temporary foetal distress imputed to the trilene occurred in 1 case only. There was no attributable foetal morbidity. The longest time of administration was 9 hours. The amount of trilene used was ½ to 1 oz. (15 to 28 ml.) in the average case. There was no difficulty in combining it with ether or chloroform when necessary. Five patients were dissatisfied, but 4 of these were temperamentally unsuited to any method of analgesia; 22 were satisfied, and 72 " very satisfied ". Analgesia with trilene was more successful than with gas and air with the apparatus set to deliver 60 per cent of nitrous oxide instead of the usual 45 per cent (the practice at this hospital), and was preferred by those who had experienced both. The average cost

was 4*d*. per case, compared with 6*s*. 8*d*. for gas and air. Portability and simplicity are further recommendations.

Ronald Woolmer

136. Addition of Penicillin Sodium to Anaesthetic Agent for Local Infiltration Anaesthesia. Preliminary Report.
By V. J. REYNOLDS. *Amer. J. Obstet. Gynec.*, 52, 641–644, Oct., 1946. 10 refs.

The author had found that the results of perineal repairs after delivery were often unsatisfactory. This was believed, after a review of all possible causes, to be due to two factors—impaired circulation and infection. To eliminate the latter the use of penicillin was considered. For 81 consecutive repairs of incisions or lacerations a local infiltration was made of 1 per cent procaine hydrochloride in normal saline, to which 250 units of freshly made penicillin sodium were added per ml. of the solution. This mixture was freshly prepared at the time of each delivery. An average of 45 ml. was injected subcutaneously, intramuscularly, and submucosally into the vulvo-vagino-perineal area by infiltration. In 2 patients pudendal nerve blocks were done, 15 ml. being injected into the area around Alcock's (pudendal) canal on each side. In 77 cases the results were excellent. While in the other 4 healing was not by first intention, there was no evidence of infection in any. The author considers the results sufficiently encouraging to warrant further study.

F. J. Browne

PUERPERIUM

137. Levels of Penicillin in the Blood after the Use in the Vagina and Rectum of Suppositories containing Penicillin Calcium: Preliminary Report.
By S. B. LOVELADY, L. M. RANDALL, and S. M. HOSFELD. *Proc. Mayo Clin.*, 21, 401–403, Oct. 16, 1946.

In a group of women in an uncomplicated puerperium, suppositories of 100,000 units of penicillin calcium were inserted into the vagina or rectum. Among 36 cases in which the vaginal route was used, concentrations of 0.06 unit or more of penicillin per ml. of blood serum were still present in the majority 3 hours after the insertion of two or three suppositories. The blood levels after the use

of one suppository were below this standard. In 33 cases in which the rectal route was used slightly lower average concentrations were obtained in the blood serum after 3 hours. The blood levels 5 hours after insertion of the suppositories were frequently below the standard level of 0.06 units per ml., and in a proportion of cases had fallen to nil. Although these results were obtained in the majority, there were some cases in both experiments in which absorption had apparently completely failed and blood levels of zero were recorded. The authors do not refer to these failures, but consider that the suppositories might be used as a routine prophylactic measure in the preparation of patients for delivery, especially where premature rupture of the membranes has occurred and before Caesarean section. They state also that the suppositories have given good results in the treatment of acute vaginitis in ambulatory patients.

[This method of prophylactic administration, while convenient, seems to be uncertain in action and somewhat wasteful of penicillin.]

H. Stanley Banks

138. The Use of a Pessary as an Adjunct to Early Rising in the Puerperium.
By C. W. PAVEY. *Ohio St. med. J.*, 42, 1047–1049, Oct., 1946. 18 refs.

The author advocates routine low forceps delivery of primigravidae and multiparae, with a median episiotomy sutured by catgut. The placenta is expressed, ergotamine tartrate is given intravenously, and a Smith-Hodge pessary is inserted. The pessary is not used when there are extensive vaginal tears because of the pain caused by pressure on abraded areas. Within 4 to 14 hours of delivery the patient is propped up erect in bed for 15 minutes and she then gets up out of bed and stands on the floor for 2 to 5 minutes. It is recommended that two nurses should be in attendance. Later the same day the patient sits up in a chair for 15 to 30 minutes, and the following day she gets up at least three times and walks about the room. On the third and fourth day she can walk about the hospital and on the seventh day she is discharged. In the author's opinion the alleged dangers of early mobilization of puerperal patients, such as prolapse, perineal wound disruption, displacement, haemorrhage, and embolism, are all reduced in incidence by the routine he advises. In

the first year of trial the procedure was adopted in 366 private patients—204 multiparae and 162 primiparae—but in only 233 were pessaries fitted. The author is enthusiastic about his results and states that with few exceptions his patients welcomed the routine. *J. Stallworthy*

139. **Pulmonary Embolism in Obstetrics and Surgery.** (El embolismo pulmonar en clínica, obstetricia y cirugía.)

By E. S. MAZZEI, D. TAYLOR GOROSTIAGA, and E. MAGALHAES. *Prensa méd. argent.*, 33, 1851–1854, Sept. 13, 1946.

140. **Electrotherapy of the Levator Muscle of the Anus (Levator Ani) during the Postpartum Period and in Some Gynecologic Conditions.**

By·H. VIGNES. *West. J. Surg.*, 54, 394–396, Oct. 1946.

Electrical stimulation of the levator ani muscles is suggested as being beneficial to women in the puerperium, and to those in whom there is weakness of the muscles. A bowled metallic electrode (1 cm. diameter) enclosed in an ebonite ball placed in the rectum and a large condensing plate (15 × 20 cm.) covered with a layer of fine felt and chamois leather are the two terminals. The stimulation is obtained by superimposing a continuous current of 12 to 25 milliamperes upon an alternating current of 5 per cent of this strength, with a frequency of 50 mA. [? per second]. Some remarkable claims are made about the benefits obtained, but no controls were used and much of the improvement seemed to be in subjective symptoms only. The value of the treatment may best be illustrated by the following quotations. A case of incipient prolapse in a recently delivered woman, aged 32, was cured after 5 treatments. Six women who came complaining of abdominal heaviness, tiredness, and impossibility of prolonged physical exercise all felt relief after 1 treatment. Four cases of incontinence of urine in women of varying ages (60, 40, 40, and 31 years) were cured after a number of treatments varying from 5 to 12.

D. M. Stern

141. **Penicillin in Treatment of Acute Puerperal Mastitis.**

By M. D. TAYLOR and S. WAY. *Brit. med. J.*, 2, 731–732, Nov. 16, 1946. 2 refs.

Taylor and Way have contributed a brief study of the use of penicillin in the treatment of acute

puerperal mastitis. They refer to the fact that the results of this type of treatment are often unsatisfactory despite the fact that, since the causal organism is the *Staphylococcus aureus*, one would expect penicillin treatment to be effective. The authors attribute the disappointing results experienced by other workers to inadequate dosage and to the use of local therapy only, and quote Vaughan Hudson's conclusion that local penicillin treatment is not successful in soft-tissue infections unless they are entirely confined to the surface—a state of affairs which does not usually obtain by the time a diagnosis of acute puerperal mastitis can be made.

Two measures are necessary for the treatment of the condition: the breast must be effectively emptied and the infection adequately controlled. The emptying of the breast should, if possible, be effected by permitting the child to feed, but, if this should prove impracticable, then suckling is temporarily discontinued and small doses of stilboestrol are administered—usually not more than 1 mg. in 24 hours. The infection can be controlled effectively only by the systemic administration of large doses of penicillin. The authors advise 3-hourly injections of 12,000 to 20,000 Oxford units. All of the 10 cases reported by the authors yielded completely to this regime within periods varying from 2 to 7 days from the beginning of treatment, and in all but 1 case lactation was not interfered with. The total dosage of penicillin administered varied from 300,000 to 1,050,000 Oxford units. While admitting that these cases represent a somewhat limited experience, the authors are confident that the treatment suggested is worthy of extended trial. *Falkland L. Cary*

142. **The Health Centre's Part in the Prevention of Puerperal Sepsis.**

By C. M. MARTIN. *J. Obstet. Gynaec., Lahore.*, 7, 127–133, Aug. 1946.

THE INFANT

143. **Prolapse of the Umbilical Cord.**
By S. B. GUSBERG. *Amer. J. Obstet. Gynec.*, 52, 826–829, Nov. 1946. 6 refs.

144. **Congenital Hyperplasia of the Islets of Langerhans in Foetuses of Diabetic Mothers.** (Kongenital hyperplasi av Langhans' öar med ökning av β-cellerna hos foster till diabetiska mödrar.)

By G. T. HULTQUIST, I. LINDGREN, and J. B.

DALGAARD. *Nord. Med.*, 31, 1841–1845, Aug. 16, 1946. 3 figs., 45 refs.

Three cases of pregnancy in diabetic subjects are described; in 1 case an improved carbohydrate tolerance was seen, which permitted reduction of the insulin dosage. The foetuses were born dead, and a histological examination of the pancreas was carried out. Sections were stained by the Gros- Schultze silver impregnation method, by which α-cells are stained and the β-cells unstained. The relative proportions of the two kinds of cells were estimated, and it was found that the proportion of α-cells was one half the normal value. New forma- tion of islets was seen, consisting mostly of α-cells, with a differentiation of islet cells into β-cells occurring mostly in the larger islets. Examina- of other foetal organs revealed fatty infiltration of the liver and kidneys with deposition of glycogen. The adrenals showed cortical hyperplasia with haemorrhage in 2 cases.

D. J. Bauer

145. Maternal Rubella as a Cause of Congenital Defects.

By L. G. PARSONS. *Brit. med. Bull.*, 4, 193–196, 1946. 10 refs.

In 1941 Gregg, an Australian ophthalmologist (*Trans. Ophth. Soc. Aust.*, 1941, 3, 35), encountered an unusual form of congenital cataract in a number of infants, and following this up in co-operation with his colleagues he was able to collect a total of 78 such cases. Frequently these babies were small at birth, ill nourished, and difficult to feed, and 44 of them suffered also from congenital heart disease. He found that 68 of the mothers of these infants gave a history of rubella during pregnancy; this disease had most often occurred during the first or second month of their pregnancy. In a footnote it is stated that Gregg has now collected a total of 206 examples of this association between mater- nal rubella and congenital defects.

Following on this observation, a survey was sponsored by the National Health and Research Council of Australia. Information concerning 74 mothers who had suffered from rubella during preg- nancy or had congenitally defective offspring was collected. Of these mothers 57 had suffered from rubella and their offspring manifested congenital defects, involving the eye, the heart, the ear, or the general mental development. Not infrequently

more than one defect was present in the same child; moreover, many of these infants were under- nourished and difficult to feed. These investiga- tors came to the conclusion that " When a woman contracts rubella within the first 2 months of pregnancy it would appear that the chances of her giving birth to a congenitally defective child are in the region of 100 per cent, and if she contracts it in the third month about 50 per cent ". A few cases have now been reported both in England and in America which lend support to this associa- tion.

[The evidence from Australian observations does support the view that these defects are due to rubella, but before it can be considered proven further statistical and other studies are required. This will not be easy, for large epidemics are in- frequent and the population at risk is small. To obtain really good statistical results it would be necessary to include in the survey *all* married women in England and Wales. A recent editorial (*Brit. med. J.*, 1946, 2, 778) states that rubella during the early months of pregnancy has some- thing less than a 10 per cent chance of damaging the foetus.]

Jas. M. Smellie

146. Congenital Deformities. (Aangeboren mis- vorming.)

By A. THOLEN. *Geneesk. Tijds.*, 24, 338–340, December 5, 1946.

147. The Toxic Diseases of the Newborn. Prelimin- ary Report.

By J. A. FREEL. *Arch. Pediat.*, 63, 440–478, September 1946. 4 figs.

The author defines toxic disease of the newborn as one caused by poisons produced by the hydro- lysis of the exotoxins of spores on the carbohy- drates, proteins, and fats present in the infant's diet. He holds that epidemic diarrhoea of the newborn is not an infectious but a toxic disease caused by the presence in the infant's food of butyric acid, acetic acid, and propyl and butyl alcohols. He brings the following evidence to sup- port this view : (1) *Clostridium butyricum* and *Bacillus subtilis* were isolated from 6 cans of evaporated milk obtained from a hospital using such milk for infant feeds during an outbreak of epidemic diarrhoea. (2) Clostridia were isolated from 39 of 40 cans of evaporated milk brought in as suspect by mothers of infants; pure cultures of the organisms were not obtained. (3) Contamin-

ated milk administered to 2 kittens produced severe symptoms. (4) Contaminated milk was found to contain fairly large quantities of acetic acid (up to 1.2 per cent) and butyric acid (up to 1.12 per cent), and small quantities of butyl and propyl alcohols. (5) Experiments on 4 kittens showed that while butyric acid given by mouth produced gastritis, isopropyl alcohol given subcutaneously in evaporated milk (5 ml. of a 10 per cent solution) caused diarrhoea, restlessness, convulsions, and coma. Similar results were obtained with butyl alcohol.

The author concludes that it is possibly the prophyl and butyl alcohols in contaminated milk which cause death in infantile enteritis. He also concludes that such diarrhoea of infancy should be treated primarily as a chemical poisoning. Hence the gastro-intestinal tract should be emptied as soon as the diagnosis is made by gastric lavage and alkaline enemata. Alkalis should also be given by mouth. He describes 3 cases treated successfully by these methods, and adds that he has treated over 100 cases in the last 3 years.

F. A. Langley

148. Persistent Vomiting in Infants Treated by Continuous Nasal Drip-feeds.

By T. N. NAUTH-MISIR. *Brit. med. J.*, 2, 737, November 16, 1946. 1 ref.

Good results are claimed for this technique, which is simple and easily mastered by trained nurses. The author uses a soft rubber catheter (size 4 to 6) which is lubricated and passed via the nose into the stomach. The prescribed feed is contained in the bottle of the standard blood-transfusion set which is then connected to the catheter. The required volume of the mixture prescribed is dripped slowly into the stomach over 24 hours or longer, a rate of 8 drops per minute delivering 20 ounces (568 ml.) in 24 hours approximately. The maximum amount of rest is obtained by this method, which can be combined with sedation; where this is indicated the food requirements of the infant can, theoretically, be maintained over a long period.

[Brenneman, however, has reported a fatal termination due to ulceration and oedema of the oesophagus following " too prolonged use " of the method without interruption.]

M. Baber

149. Modification of the Ericson and Johnson Resuscitator.

By C. W. PAVEY. *Amer. J. Obstet. Gynec.*, 52, 867–868, November 1946. 1 fig.

150. Spontaneous Pneumothorax in the Newborn.

By E. P. SCOTT and C. C. ROTONDO. *Amer. J. Dis. Child.*, 72, 207–210, August 1946. 3 figs., 12 refs.

The authors report a case of spontaneous pneumothorax, occurring in a 5-day-old infant delivered by Caesarean section, and refer briefly to the literature of this condition as it occurs in newborn infants. Case reports are relatively rare, but in one series of routine radiographic studies of 702 newborn infants Davis and Stevens (*Amer. J. Obstet. Gynec.*, 1930, 20, 73) reported finding 6 instances of spontaneous pneumothorax. Clinical signs and symptoms may easily be overlooked. Trauma during delivery is presumed to play a major part in causation, but 5 other cases have been reported where the infants were delivered by Caesarean section. The infant described was a girl, apparently full-term, delivered by Caesarean section under spinal analgesia on account of placenta praevia. At birth she was cyanosed but breathed normally, and resuscitation consisted of extraction of mucus only. On the fifth day of life she was found to have a temperature of 103.6°F (39.8°C.) and to be dehydrated. Her weight had dropped by 19½ ounces (553 g.). She was again cyanosed and lethargic, and had one mild convulsion. Examination failed to reveal any abnormal signs, but a skiagram of the chest showed a right pneumothorax. Oxygen was given for 2 days with treatment for dehydration, and gradual improvement followed. Five days after the first X-ray examination the chest was found to be normal radiographically. It is emphasized that treatment should be conservative.

M. Baber

151. Icterus Gravis Neonatorum. End-results of Treatment by Blood-transfusion.

By H. THIRD. *Lancet*, 2, 635–636, November 2, 1946. 6 refs.

The end-results of treatment by blood-transfusion of 6 infants suffering from icterus gravis neonatorum are given. At the time of the review the average age of the babies was 18 months. In 4 cases the father's blood was Rh-positive and the mother's Rh-negative with Rh antibodies in the

maternal serum. There was also a typical family history in each case, one or more normal infants being followed by affected siblings. The other 2 cases were in twin girls; the blood of both parents was Rh-positive (father, A R R; mother, O R R). No antibodies were found in the maternal serum. The mother had previously given birth to a still-born anencephalic monster followed by a miscarriage at 3 months. For transfusion, group O Rh-negative blood was used until the relevant typing was completed, the amount of blood given being 10–20 ml. per pound of body weight. Artificial feeding was used. Of the 6 infants, 3 became normal healthy babies, 1 was an imbecile, 1 was suspected of spasticity and backwardness, and 1 of the twins also became spastic and backward.

<div style="text-align:right">F. A. Langley</div>

152. A Summary of Present Knowledge of Human Blood-Groups, with Special Reference to Serological Incompatibility as a Cause of Congenital Disease.
By R. R. RACE. *Brit. med. Bull.*, 4, 188–193, 1946. 6 figs., 42 refs.

The author stresses the fact that haemolytic disease of the foetus and newborn child is almost always due to Rh group incompatibility, but quotes the few rare exceptions. He also casts doubt on the conclusion of some American authors that there is any abnormal Rh-group distribution of mothers of primary mental defectives.

[This is a very concise and lucid summary with examples of the effect of blood group incompatibility on babies and should be valuable to all clinicians interested in the subject.]

<div style="text-align:right">John Murray</div>

153. The Blood Group Rh. I—A Review of the Antigenic Structure and Serological Reactions of the Rh Subtypes.
By D. F. CAPELL. *Brit. med. J.*, 2, 601–605, October 26, 1946.

The Blood Group Rh. II—Clinical Applications in Transfusion Therapy and in Haemolytic Disease of the Newborn.
By D. F. CAPPELL. *Brit. med. J.*, 2, 641–647, November 2, 1946. 59 refs.

The author discusses the discovery of the immune agglutinins of the Rh system. He suggests the replacement of Wiener's cumbersome terminology by Fisher's neat designations. Fisher suggested that in each individual the Rh pheno-

type is determined by 3 closely linked pairs of allelomorphic genes—Cc, Dd, Ee. This triple gene complex gives rise to 8 theoretical Rh types, and 7 have been found—Rh_1 (CDe), Rh_2 (cDE), Rh' (CDe), Rh" (cdE), Rh_z (CDE), rh (cde), Rh_0 (cDe). The 8 possible types of genes allow of 28 possible genotypes. The products of the triple gene complex should give rise, theoretically, to 6 antibodies, and 5 have been found. It is emphasized that the D antigen is the only really common cause of sensitization, either in intragroup transfusion reactions or in pregnancy. The anti-D-immune serum reacts with 85 per cent of human cells, all of which are Rh-positive (standard Rh serum, anti-Rh_0 serum). Anti-C serum reacts with 70 per cent of all cells and made it possible to designate the Rh' subtype (anti-Rh' serum). Anti-E serum reacts with 30 per cent of all cells and permitted the identification of the Rh" subtype (anti-Rh" serum). Neither the Rh' nor the Rh" subtype reacts with the standard Rh serum. Anti-c serum reacts with Rh-negative cells and detects the Rh-negative factor also in the heterozygous Rh_2 cells anti-Hr St serum). Lately Mourant discovered the anti-e serum. Although Fisher's scheme is very attractive and essentially correct, new work showed it to be oversimplified. Callender, Race and Paykoç found an antibody (anti-Willis) which reacted with a second allelomorph at the Cc locus, called C_w. Almost 50 per cent of anti-C sera react with both C and C_w, whereas the others react only with C. It was also observed that some of the sera may contain 2 or more antibodies of the types described. The author warns against the designation as Rh-positive of persons of the Rh' and Rh" subtypes. If such subjects receive a transfusion of Rh-positive blood they may develop the dangerous anti-D antibody. On the other hand, their blood may not be listed as Rh-negative as it may give rise to incompatibility reactions when transfused into patients with anti-c or anti-E antibodies. The author suggests that they should be eliminated from a panel of Rh-negative donors; but regarded as Rh-negative recipients.

The author then proceeds to discuss the " incomplete " or " blocking " antibody. Maternal sera may contain antibodies which interfere with the agglutination of human cells by their appropriate immune-agglutinin, but which do not lead to agglutination by the ordinary methods. Dia-

mond and Abelson determined those incomplete antibodies, however, by suspending the test cells in compatible serum or in 30 per cent serum albumin. Coombs, Mourant, and Race showed that the union of the blocking antibodies with Rh-positive cells could be demonstrated by washing treated cells free from serum and then adding anti-human-globulin serum, when prompt agglutination took place (indirect test). They also showed that cells sensitized *in vivo*, as is the case in haemolytic disease of the newborn, are agglutinated by the anti-human-antibody-globulin serum when washed free from their plasma (direct test). The blocking antibodies may appear in the maternal serum instead of agglutinating antibodies, and may affect the foetus severely. They are considered to be a bad prognostic sign.

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An Rh-negative recipient may become immunized by transfusions of Rh-positive blood. Whereas the first transfusion may be symptomless, further transfusions may be followed by progressively severe symptoms. The administered Rh-positive blood contains the antigens C and/or D and/or E. It is usually the antigen D which is effective. The resulting anti-D antibodies may be accompanied by blocking anti-D antibodies, so that agglutination is only apparent when special tests are carried out (see Part I). In some cases anti-D and anti-C agglutinin may develop. In such instances a blocking anti-D antibody may mask the agglutinating anti-D, so that the serum appears as a homospecific anti-C serum unless the blocking tests are carried out. The antigen E rarely gives rise to antibodies. The author stresses the point that females in or before the reproductive period should receive only blood of Rh type similar to their own. Once sensitization has been established it may give rise to reactions after many years, thus causing haemolytic disease in subsequent pregnancies. The Rh type should be ascertained before each transfusion if time is available. Rh incompatibility is by far the most important cause of foetal death. Haemolytic disease may be expected in about 1 in 250 births. Iso-immunization is more likely to occur where the father is homozygous Rh-positive, but it is not rare with heterozygous fathers.

Results of investigations in 114 cases of haemolytic disease of the newborn are given. Ninety-eight out of 114 mothers were Rh-negative, and 86 out of 98 had antibodies. Sixteen out of 114 mothers were Rh-positive, and only 2 out of 16 had antibodies recognizable by the ordinary saline dilution method. The author believes that some antibodies were missed, as the blocking tests were unknown at the time of the investigations. In only 4 out of 114 mothers was the disease proved in the first pregnancy, and one of those was a dizygotic twin pregnancy. In some families haemolytic disease appeared after 10 or more pregnancies. The author has not encountered a single case where a normal healthy Rh-positive child has been born to an Rh-negative mother after haemolytic disease has occurred in her early offspring. He also records 37 multiparae who had not lost a single child. He admits that we do not yet know why some Rh-negative mothers react so quickly and others more slowly to the Rh antigen. He considers the aptitude to become sensitized to be also an inherited factor. On the other hand, the occurrence of haemolytic disease may be influenced by heterospecific pregnancies. The infant is more likely to be affected when its ABO group is compatible with the mother's. Only 8 out of 90 affected pregnancies were heterospecific, whereas 82 were homospecific. The random distribution should be 18 to 72.

The treatment of haemolytic disease consisted of transfusion at the earliest possible moment: 150 ml. of blood were usually given, either once or twice. Transfusions were carried out slowly. The blood chosen for the infant must not be susceptible to the antibodies present in the mother's serum. In the majority of cases the mother will be Rh-negative and will possess anti-D antibodies. In that event the infant should be transfused with Rh-negative blood, of group O or of the homologous group to the infant's blood.

The paper gives the records of 12 cases of Rh immunization during pregnancy.

Kate Maunsell

154. Hemolytic Disease Associated with the Rh Factor in Twin Pregnancies.
By E. A. CONTI and J. W. GLENN. *Amer. J. Obstet. Gynec.*, 52, 446–450, September 1946. 11 refs.

The incidence of haemolytic disease of the newborn resulting from the deleterious effect of trans-

mitted maternal antibodies is difficult to determine. The combination of an Rh-negative wife and an Rh-Positive husband occurs once in about thirteen marriages of white people (in America). However, as individuals differ in the ease with which they can " be sensitized ", only about 1 in 25 to 50 Rh-negative persons exposed to the Rh antigen " becomes sensitized ". Occasional occurrences of haemolytic disease when the mother is Rh-positive have been attributed to subtypes of Rh and the Hr factor. Blocking antibodies are probably more significant than agglutinating antibodies of haemolytic disease because they are smaller and hence traverse the placental barrier more easily.

The study of cases of erythroblastosis occurring in twin pregnancies is interesting. Stratton, Langley, and Lister reported the twin pregnancy of an Rh-negative woman; both twins were Rh-positive but of different genotypes. The female was normal, but the male died of haemolytic disease on the fourth day. Aaburg and Roby described a heterozygous pregnancy which presented two varieties of erythroblastosis (icterus gravis and hydrops). Both twins were Rh-positive and the mother was Rh-negative. Thus a difference is shown in the effect on twins of Rh antibodies. Wiener reported a twin pregnancy in which the male twin was Rh-negative and normal and the female died of icterus gravis within 13 hours.

The authors, from a series of 110 multiple pregnancies, report upon 6 twin pregnancies showing evidence of erythroblastosis, 3 in Rh-negative and 3 in Rh-positive women. The first case was in an Rh-negative primigravida; the first child, a normal healthy male, was Rh-negative but the second child, a female, showed a typical picture of hydrops foetalis. The second case was also an Rh-negative primigravida; at full term she had an anaemic Rh-positive male child which survived and at 3½ years was physically normal but mentally about 6 months old. The second twin, also male, was a macerated foetus with oedematous body and shapeless cranium. The third patient, also Rh-negative, had normal heterozygous twins in her first pregnancy, both Rh-positive; 2½ years later she had homozygous twins born prematurely. The first female of the second set of twins had moderate anaemia, but survived and is apparently normal at 3½ years of age. The second child presented the typical features of an icterus gravis, thus again

demonstrating the varying response to antibody exposure (or accessibility to the maternal antigens) this time with the more common feature of erythroblastosis—initial sensitization by the first set of Rh-positive twins.

The next 3 cases were in Rh-positive women. The fourth patient had a spontaneous abortion after giving birth to a normal Rh-positive female child. Then homozygous twins were born at 34 weeks. The stillborn female was small with parchment-like yellow skin—foetus papyraceus. The survivor with disproportionately large head and wide fontanelles is physically normal at 18 months but mentally backward. Both were Rh-positive but full serological typing was not possible. The twin pregnancy in Case 5 was preceded by the delivery of a normal Rh-positive foetus 2 years earlier. The second twin, of the reported pregnancy, was a normal Rh-negative male; the other, a male, had a large head and wide fontanelles and died at 11 days after bleeding from mucous membranes for 9 days. Rh determination was not done, but the baby is considered to have been Rh-negative as the pregnancy was monochorial, and the authors believe that the haemorrhagic disease in this case can be explained by the Hr factor. The last case the authors would also explain as due to the operation of an Hr factor— 2 normal Rh-positive children preceded twins which were Rh-negative and homozygous; the male survivor (aged 6) was smaller at birth, the larger died at 36 hours from intracranial haemorrhage which is considered to be a manifestation of haemolytic disease.

[It is regretted that the value of this interesting paper is reduced by the limited nature of the serological work which was possible.]

J. F. Heggie

155. Outlook for Infants receiving Anti-Rh Agglutinins from Iso-immunization of Mothers.
By A. BLOXSOM. *Tex. St. J. Med.*, 42, 279–281, August 1946. 7 refs.

Rh-positive cells were incubated with various random Rh-negative and Rh-positive sera of the same ABO group. Anti-Rh immune testing serum was then added to incubated cell-serum suspension. It was observed that the agglutinin titre of the immune serum differed according to the serum used for the cell-serum suspension. It was much

lower when certain Rh-negative sera were used for the cell-serum suspensions. The author assumed that those sera contained an anti-Rh reacting factor. He then studied the presence of the anti-Rh reacting factor in 5 sera of Rh-negative mothers and their Rh-positive infants. Infant A was a normal Rh-positive child and the result of a first pregnancy. The mother had a high amount and the infant a low amount of anti-Rh reacting factor. [The stage at which the blood was taken is not mentioned.] Infant B was a fourth child, the third infant having died of erythroblastosis. Seven days before delivery of infant B the mother's blood showed anti-Rh agglutinins and an anti-Rh factor at a titre of 1 in 32. Twelve hours after delivery there were no anti-Rh agglutinins demonstrable but the anti-Rh reacting factor had increased fourfold. Infant B—a normal baby—showed weak anti-Rh agglutinins after delivery and the same titre of anti-Rh reacting factor. Infant C was delivered dead of erythroblastosis. Neither the mother nor the child showed anti-Rh reacting factor. Infant D died of erythroblastosis on the seventh day. Mother and infant had a weak titre of anti-Rh reacting factor. The anti-Rh reacting factor differed from the " blocking antibody " because it occurred also in serum of unsensitized male Rh-negative donors. It was concluded that the anti-Rh reacting factor might be the essential protection against erythroblastosis. The suggestion is made that regular transfusions of serum containing this factor be given to sensitized Rh-negative mothers during gestation.

[The hypothesis of an Rh protecting factor occurring in Rh-negative sera is certainly very attractive. The author, however, does not give details on technique, regarding which a reference is given to Bloxsom and Matthaei, *Amer. J. Dis. Child.*, in the press. Before this paper is available no comment can be made.]

Kate Maunsell

156. **Technique for Determining Rh Factors** (Tecnica per evelare lo " Stato Rh ".)

By M. Tortora. *Arch. Obstet. Ginec.*, **51**, 230–244, July-August 1946. 24 refs.

157. **Some Clinical Aspects of the Rh Factor in Obstetrics.**

By E. L. King and J. W. Davenport. *Amer. J. Obstet. Gynec.*, **52**, 917–925, December 1946. 20 refs.

158. **Some Aspects of Protein Metabolism in Infants and Children.**

By F. W. Clements. *Med. J. Aust.*, 2, 404–409, September 21, 1946. 6 figs., 43 refs.

The amount of protein available for the muscles depends on the demands of certain high priority tissues—red blood cells, liver, intestinal muscles—which have to be met first. If protein intake is poor the skeletal muscles must go short first. If the deficiency is prolonged and severe all tissues will suffer, and the serum protein will fall. Cows' milk contains much more protein than human milk, but the breast-fed baby retains more nitrogen. Occasionally breast milk has a protein content below the average, and the baby will then show poor muscle tone, and, what is more important, a diminished immunity owing to the deficiency in γ globulin. Thus the level of protein reserve in the infant's body should be kept as high as possible.

Artificially-fed infants under 10 months of age must have a relatively higher protein intake than breast-fed children if they are to obtain the same quantity of essential amino-acids. This is provided in the common methods of feeding. If, however, the normal consumption of protein is interfered with in any way, then the supply of protein components in the metabolic pool must be drawn solely from the labile protein of the skeletal muscles. The child's weight then remains stationary or diminishes, the muscles become soft, and the face drawn and bluish. In these cases additional protein is indicated in convalescence, and a mixture (No. 1 protein mixture) of fine casein (90 mesh) and dried skim milk (equal parts) has been used with success (1 tablespoonful contains 6 g. of protein and 2.2 g. of sugar). Half a teaspoonful is given with each normal feed to begin with, and this is increased to 1½ to 2 teaspoonfuls with each of five feeds. Enough water is mixed with the powder to make a fairly thick gruel.

Two cases are described. One infant, a healthy 4-weeks-old breast-fed baby, was fed on glucose and water only for 5 days during his mother's illness, and was then returned to the breast. Although there was plenty of milk it was found on the eighth day that he had lost 18 ounces (510 g.). The child was given 10 to 15 grammes extra protein a day and the weight was regained in a week. The second infant, who was 9 weeks old and weighed 7 pounds 1 ounce (3.2 kg.) had been

fed on various weak milk mixtures. No. 1 protein mixture was given in a 50 per cent milk mixture. The gain in weight and clinical improvement were spectacular, and by the eighteenth week the infant's weight exceeded the average.

Older children receiving 3 meals a day are more liable to suffer from protein deficiency than infants. They require 3 to 4 grammes of protein per kilo per day, or 40 grammes per day for a " toddler." This is provided by: milk, 24 ounces (720 ml.) a day; meat, 1 chop or 1½ ounces (42.8 g.) of chopped steak, or 1½ ounces of fish per day; eggs 4 a week; bread, 1 slice a day; cereals, half a cupful a day; potatoes, 2 tablespoonfuls a day; mixed vegetables 3 tablespoonfuls a day. This standard is often not reached with consequent interference with growth. Many mothers fear to give meat to young children, except brains, which have relatively low protein content. In 25 children there were poor muscle tone and unsatisfactory growth, and an accurate assessment of the diets of 7 of them, aged from 12 to 24 months, showed grave deficiency in protein intake. With thiamine and riboflavin treatment there was no improvement, so a high-protein diet was given by including the following mixture (No. 2 protein mixture): Commercial casein, 60 per cent; dried skim milk, 20 per cent; powdered wheat germ, 10 per cent; maize protein, 10 per cent; One level teaspoonful of this powder contains 7 grammes of protein. One teaspoonful daily was given at first, increased by 1 teaspoonful daily until 4 teaspoonfuls were being taken. It was given with 2 or more ounces (70 ml.) of milk. The mixture was cooked for 1 minute and sugar, tomato juice, and a little salt were added. There was dramatic all-round improvement in 20 of the 25 children with large gains in weight.

Lack of appetite is one of the earliest signs of protein deficiency. Children have a high tolerance for protein, and although, theoretically, there is increased work for the kidneys when much is ingested, it is very doubtful if a high-protein diet has any deleterious effect on these organs in childhood.   *J. Vernon Braithwaite*

159. Prevention of Infant Deaths. Liaison between Hospitals and Home Services.
By J. T. Lewis. *Brit. med. J.*, 2, 893–985, December 14, 1946. 18 refs.

The author discusses those cases in which infants die soon after they leave the maternity units and hospitals where they were born, and considers how such deaths may be prevented by more effective liaison between the medical and nursing services in the institution and in the home. Seven case histories are described, with comments on the particular factor accounting for death. In each case death was due directly or indirectly to lack of " mothering " and care after the infant left the institution. This home care is more necessary in premature and weakly infants, but is needed also in healthy infants. The ideal solution where home conditions are adverse is the provision of special hostels for mothers and babies or a longer stay in the maternity home. The author discusses the two questions: lack of accommodation and the dangers of cross infection. He states that the alternatives of danger from cross-infection in hospital and the hazard of grossly unsuitable home conditions must be carefully balanced by the hospital doctor and the medical officer of health. But to achieve good liaison the usual notice to the public health department of discharge of the baby, with a short clinical report and a request for an early call by the health visitor, is not enough. He describes a scheme which he has introduced in his area (Barnsley), and which includes the following: (1) The unofficial reporting of pregnancies to the health department by antenatal clinics and domiciliary midwives. (2) Early investigation of the social, economic, and environmental conditions of the families and households concerned. (3) Ascertainment as early in the pregnancy as possible of households needing observation and the maintenance in the public health department of a list of such households. (4) Attempts to ameliorate adverse conditions where found. (5) The checking against the list of all notifications of birth as soon as received. (6) The reporting of home conditions to the hospital doctor immediately after the birth in hospital of a baby to an " observation " household. (7) The reporting to the health department of all admissions to hospitals of babies under 1 year, and, where the infants are from " observation " households, the reporting of home conditions to the hospital doctor. (8) A discussion, when babies from " observation " households are ready for discharge, between the hospital doctor and the medical officer of health, with special reference to the alternatives of hospital cross-infection and

adverse home conditions. This scheme places the onus for initiating liaison on the public health department.

[The part to be played by the family or home doctor in liaison is not mentioned.]

C. McNeil

160. **The Post-Mortem Examination of the Newborn Infant.**
By H. S. BAAR. *Brit. med. Bull.*, 4, 178-188, 1946. 14 figs., 59 refs.

The author does not accept the generally recognized definition of the neonatal period, but extends it to the first 3 months of life. His primary purpose is to describe in great detail the technique of post-mortem examination of the infant. *Pari passu* with this goes an accurate description of almost all the common, and many of the rare and unusual, congenital abnormalities, injuries, and diseases of this period of life. Aetiology and differential diagnoses are described at length, and the importance of accurate bacteriological and histological investigation is stressed.

[This is a lengthy and comprehensive article with an incomplete title. It is not suitable for abstraction, but must be read in the original.]

Jas. M. Smellie

161. **The Pathology of Stillbirth and Neonatal Death. A Review of 1,053 Cases.**
By A. R. MACGREGOR. *Brit. med. Bull.*, 4, 174-178, 1946.

The problem of neonatal mortality can only be solved satisfactorily by pathological study. Clinical diagnosis of the cause of death is liable to be inaccurate, and therefore close co-operation between pathologist and clinician is of paramount importance. This review is based on experience as a pathologist to a large maternity hospital, and presents pathological findings in 435 cases of stillbirth, and 618 cases of neonatal death arranged according to the presumed principal cause of death. The majority of cases of stillbirth fall into one of three main categories: defects of development, asphyxia, and intracranial haemorrhage, while in cases of neonatal death a fourth important group is added—infective diseases. These four categories are important, in that they include over 80 per cent of both stillbirths and neonatal deaths, and are dealt with in detail.

Developmental defects of various conditions were found in 20 per cent of the stillbirths and 10.5 of the neonatal deaths. As many of these defects are not preventable their interest is embryological rather than pathological or clinical.

Asphyxia accounted for 37.2 per cent of the stillbirths and 13.1 per cent of the neonatal deaths. Stresses of birth or accidents—ante-partum haemorrhage or prolapse of the cord—are among the most important causes. A considerable quantity of liquor amnii in the lungs is a common finding at necropsy.

Intracranial haemorrhage was responsible for 24.1 per cent of stillbirths and 27.6 per cent of neonatal deaths. Three types are recognizable: subdural, subarachnoid, and intraventricular. A common site of injury is the tentorium cerebelli; a vein in its free margin is often torn and a subdural haematoma results. While the majority of these cases are full-time infants, the proportion in premature infants is high. Subarachnoid haemorrhage is encountered less frequently. Its incidence is greater in premature than in full-time infants, and it is probably due in part at least to venous engorgement of asphyxial origin. It is probably seldom in itself a direct cause of death. Intraventricular haemorrhage is much more serious, and is almost entirely a disease of the premature. Of 156 such cases studied by the author, only 7 occurred in full-time infants. The source of the haemorrhage is usually a vein in the floor of one of the lateral ventricles.

Pathological study has revealed the immense importance of infection as a cause of neonatal death. Out of 241 neonatal deaths occurring after the third day of life 65.5 per cent were due to infection. These infections usually arise in the respiratory or alimentary tract. Pneumonia is the most important and most common. In the first week of life it tends to arise in lungs in which some pathological process has developed following birth stress. In the later neonatal period these infections may be caused by the common pathogens of the respiratory tract, such as organisms of the *E. coli* group or staphylococci. Aspiration pneumonia due to the inhalation either of milk or of regurgitated gastric contents is another form of infection. Of infections of the alimentary tract, gastro-enteritis may be an epidemic disease possibly due to a virus. Thrush infection may also assume a severe and dangerous

form in the new-born baby. Other infections are relatively uncommon. Of the miscellaneous conditions haemolytic disease is the most important, and a brief description of the various pathological types is given.

One fact that emerges clearly from the writer's study is the outstanding importance of prematurity as a factor in foetal and particularly in neonatal mortality. Fifty-four per cent of the stillbirths and 70.5 per cent of the neonatal deaths occurred in cases of premature birth. During the period covered by this series of cases, slightly over 10 per cent of all live births in the hospital were premature, and it was this 10 per cent that produced almost three-quarters of the neonatal mortality. " Nothing could make a greater contribution to a reduction in the neonatal death rate than prevention of premature births."

Jas M. Smellie

162. **Vital Statistics of Stillbirths and Neonatal Deaths.**
By B. WOOLF. *Brit. med. Bull.*, 4, 170–173, 1946. 9 refs.

By reference to the Decennial Supplement (1931) and the Annual Statistical Reviews (1931 to 1940) of the Registrar-General for England and Wales and the Annual Reports of the Registrar-General for Scotland (1939 to 1943), the author analyzes the stillbirth and neonatal mortality experience of those countries in the years immediately preceding the war.

Approximately half the deaths in the first year of life in England and Wales prior to 1939 were attributable to congenital causes (which in the main occurred during the first 4 weeks of life), resulting in a rate of 30.86 deaths of infants under 1 year of age per 1,000 live births, of which prematurity accounted for 16.83 and malformations 6.02 per 1,000. It is demonstrated that among legitimate infants mortality from prematurity and congenital debility increased as social status became lower; the remaining congenital causes of death showed very little variation between social classes. In the large burghs of Scotland stillbirth rates also increased as the social scale was descended.

In Scotland during the year 1939 to 1943 the mean annual stillbirth rate due to conditions affecting the mother was 10.1, from difficult labour 9.9, from foetal malformations 6.3, and from all other causes 13.3 per 1,000 total births. In Scotland the annual infant mortality rate, assessed on total births, from congenital malformations was also 6.3 per 1,000 during the same period; thus the total wastage due to congenital malformations can be assessed at an annual figure of 12.6 stillbirths or deaths per 1,000 total births.

From data relating to England and Wales for single births only it is demonstrated that within each birth parity group the stillbirth rate increased with increasing age of mother; while within each age group of mother the stillbirth rates were at a maximum for the first child, a minimum for the second, and thereafter increased gradually with increasing birth parity. An analysis of the sex ratio of stillbirths in Scotland (1939 to 1943) revealed a male excess in all cause groups except that of foetal malformations; within this group considerable variation in the sex ratio was observed —a fact also true of infant deaths due to congenital malformations in England and Wales (1931 to 1935).

Attention is drawn to the limitations of (a) examining the problem in terms of mortality rather than morbidity, and (b) using published statistics in an analysis of this nature, particularly with reference to the examination of the influence of economic and social factors; thus it is not possible to analyze the results, according to social class, of such biological factors as have been mentioned. It would appear that malformations present a somewhat different picture from the other causes of mortality examined, and it is suggested that there is evidence that this type of mortality depends upon intra-uterine environment and not upon gene interactions at fertilization, since it is observed that (a) such mortality is high where women are engaged in onerous occupations during pregnancy; (b) mortality from congenital malformations and neonatal mortality generally is at an abnormally low level in the area of Greater London; and (c) as demonstrated for Scotland (1939 to 1943) the stillbirth rate from foetal malformations shows considerable variation with age of mother. A short discussion of other work on the influence of maternal nutrition and medical care is also included.

A. E. Cheeseman

163. Milk Embolism in the Lungs as a Cause of Rapid and Unforeseen Death in Infants. (Sur une cause de mort rapide et imprévue du nourrisson: l'embolie de lait dans le poumon.)

By J. MARIE, P. SERINGE, and S. J. MARIE. *J. Méd. Paris,* **66,** 126, Aug. 1946.

As the result of three post-mortem examinations the authors demonstrate a little-known cause of unforeseen death in infants — namely, milk embolism of the air passages. They describe: (1) The characteristic histological appearance of milk in the bronchi and alveoli (debris stained by Sudan III and curds in the alveoli, appearances which they reproduced in animal experiments): (2) Results of aspiration of milk during life into the lungs (areas of emphysema, and in one case bullae and ruptured alveolar walls). (3) The complications of milk embolism, in one case a fulminating broncho-pneumonia following regurgitation in an infant of 4 (? days). (4) The mechanism of the penetration of milk into the bronchial tree. The prevention and treatment of these accidents are also discussed.

M. Baber

See also No. 102.

MATERNAL WELFARE, MORTALITY

164. Maternal Welfare and the Negro.

By P. F. WILLIAMS. *J. Amer. med. Ass.,* **132,** 611–614, Nov. 16, 1946. 8 refs.

165. Consideration and Analysis of Maternal Mortality. [In Russian.]

By S. P. VINOGRADOVA. *Pediat. Akush. Ginek.,* No. 4, 19–24, 1946.

This article describes the system of estimating the causes of maternal mortality in the Soviet Union, and the steps taken to improve the maternity services throughout that country. A maternity service may be considered as well run when there is a decrease in maternal mortality and morbidity. Since the establishment of special committees, maternal mortality in the U.S.A. has dropped by 33 per cent. In the U.S.S.R. scientific control of maternal mortality was first introduced in 1938 by Professor Lourier, when a uniform set of obstetric procedures was adopted. Under this system the maternal mortality among 100,000 cases, treated in 50 different maternity hospitals in the Ukraine in 1941, was as low as 0.18 per cent, including a 0.06 per cent mortality due to sepsis. The international classification considers maternal *mortality* according to the causes of death, and this classification has been provisionally adopted by the Soviet Union (but the author thinks that it might be better to classify maternal mortality under the different types of treatment given and procedures carried out). Maternal mortality is regarded as including all deaths due to pregnancy or childbirth, or taking place during the puerperal period, but only if the pregnancy was one with a viable child. Deaths due to abortions, ectopic gestations, and other abnormalities are not included.

The organization for the study and control of *maternal mortality is described as follows:* The staff present a full report on each fatal case to a committee composed of specialists, which considers the case and discusses it with the medical personnel concerned. If any error in technique is detected the medical officer and the midwife are taught the correct technique. In addition, the members of the committee are responsible for actual help, when requested, in the diagnosis and treatment of any case (this includes the supply of necessary drugs and blood for transfusion). The method of analyzing maternal mortality is based on accurate certification of the cause of death, together with a detailed history of the case and careful consideration of all factors which may have been responsible for the fatal outcome. Special record is made of the method of antisepsis employed during pre-natal examinations, of the actual treatment of any infection (pharyngitis, rhinitis, pyoderma) of the mother, and of any contact of the expectant mother with infectious illnesses. The aseptic ritual followed during the labour is investigated, especially where there has been manual removal of the placenta; all manipulations, such as insufflation of sulphonamides or blood transfusion are mentioned. Special care is necessary in the analysis of operative deliveries; the length of labour, the qualifications and experience of the surgeon, and any prophylactic therapy—especially if pyrexia was present—must be stated. Importance is attached to early diagnosis of all complications and to full laboratory investigation. Any consultation with a competent specialist and any discrepancy between

the clinical diagnosis and the pathological findings must be specially noted. In deaths from toxaemia the time when the diagnosis was established and the method of treatment are carefully studied. If death occurred from cardiovascular disease, tuberculosis, or any other condition aggravated by pregnancy, the reason why the pregnancy was not terminated is investigated. The author concludes that by thorough and careful pre-natal examinations, by having available skilled personnel and all necessary appliances (such as blood-transfusion apparatus) at a moment's notice, and by the education of both the mother and the medical personnel, maternal mortality in cases in which it can be prevented by proper and timely treatment will be considerably reduced.

Nicholas Tereshchenko

OBSTETRIC OPERATIONS

166. **Prophylactic Intraperitoneal Sulphanilamide in the Surgery of the Infected Obstetric Case.** (La sulfanilamida intraperitoneal prolifáctica en la cirugía obstétrica del caso impuro.)
By M. L. Perez and R. Echevarria. *Obstet. Ginec. latino-amer.,* 4, 477–532, July 31, 1946. 4 figs., 87 refs.

In a review of over 700 Caesarean sections performed on infected cases and taken from the literature of the Argentine and other countries, and from the authors' own cases, it is concluded that the mortality in these cases is greatly reduced by the use of prophylactic sulphanilamide. The mortality in sulphanilamide-treated cases was 0.81 per cent, as compared with 4.3 per cent in controls not receiving sulphanilamide. The mortality in another series of 613 cases of lower-segment transperitoneal section treated prophylactically with sulphonamides was only 0.32 per cent; this compares very favourably with the results of extraperitoneal Caesarean section, where the mortality was 3.33 per cent.

The authors describe the results in 102 Caesarean sections in infected cases and give a detailed case history for each operation as an appendix to their article. There were no deaths from peritonitis, but 5 deaths occurred from other causes—1 from sulphanilamide intoxication, 1 from bronchopneumonia, 1 from a perforated duodenal ulcer,

and 2 from transfusion accidents with plasma. The mortality is computed on 96 out of 102 cases, and was thus 5.2 per cent. Using Sureau's classification, 68 out of the 96 cases fell into group II, 21 into group III, and 7 into group IV. In addition to intraperitoneal sulphanilamide, the drug was given directly into the uterus 4 hours after operation. The result was that the concentration in the blood rose to 18 mg. per 100 ml.; morbidity was reduced from 58 per cent with intraperitoneal sulphanilamide alone to 25 per cent. When penicillin was given in addition to intraperitoneal and parenteral sulphanilamide the morbidity fell to 14.2 per cent.

The authors recommend that, for the infected case, lower-segment Caesarean section should be performed with the minimum of trauma and the minimum of peritoneal soiling. Four grammes of sulphanilamide powder should be distributed along the suture line in the uterus, in the peritoneal cavity, and the parietes, with the greater part in the true pelvis. Parenteral sulphanilamide should be given during the 72 hours after the operation, and the level in the blood should be watched and maintained at 6 mg. per 100 ml. Penicillin should be given during or before the operation and maintained after it, 200,000 units being distributed over 48 hours. It is claimed that the problem of Caesarean section for the infected case has been solved.

[The problem of Caesarean section in infected cases is one which has long proved difficult, having been associated with high maternal mortality and morbidity. This article represents an attempt to solve this problem by means of chemotherapy. The chief weakness of the case presented is that no bacteriological studies have been made. The weakness of " blunderbuss " chemotherapy of this kind is that, unless the infecting organism is known, it is impossible to evaluate results. Also, it is known that the modern chemotherapeutic agents are not effective against all known pathogenic bacteria. The colon bacillus found frequently in infections of the genital tract is notably resistant. Doubtless chemotherapy of this kind will do something to lower morbidity and mortality from infection— though the mortality from other causes seems high in this series—but it cannot be agreed that the problem is solved.]

Josephine Barnes

167. The Extraperitoneal Caesarean Section.

By P. H. OOSTERHAGEN. *S. Afr. med. J.*, **20**, 712–713, Nov. 23rd, 1946. 10 refs.

168. A New Modification of the Technique of the Caesarean Section. [In English.]

By A. M. RITALA. *Acta obstet. gynec. scand.*, **26**, 604–609, 1946. 8 figs., 13 refs.

See also No. 133.

GYNAECOLOGY

169. Low Back Pain in Women. (Die Kreuzscherzen der Frau.)

By J. WEGLEITER. *Wien. klin. Wschr.*, **58**, 649–652, Oct. 25, 1946.

170. Psychosomatic Gynecology.

By J. P. PRATT. *J. med. Ass. Georgia*, **35**, 243–256, Sept., 1946. 8 refs.

In this article Pratt affirms his belief in the importance of the psychosomatic element in the diseases of women. He illustrates this by references to cases seen in his own practice. The woman who blames an operation for the symptoms produced by the death of an intimate friend is given as an example. He stresses the need for kindly talks before operation as a means of diminishing operation fears, and cites the case of a woman who feared an anaesthetic because she had the worry of an earlier abortion on her mind. He describes a case of dysmenorrhoea caused by anxiety over masturbation, and a similar one produced by the psychic trauma of overhearing a maid having intercourse and later being threatened with murder by the maid if she mentioned it. Again he points out that symptoms are often attributed to the menopause which are really the result of the emptiness and aimlessness of life consequent upon the growing up and leaving home of a woman's children. He deals with all these difficulties in a superficial way, but no doubt his insight and kindly approach are very helpful to those who do not need deeper psychological exploration.

Clifford Allen

Menstrual Disorders

171. Menstrual Disorders. Some Aspects of Sex Endocrinology in General Practice.

By E. C. HAMBLEN. *North Carolina med. J.*, **7**, 533–539, Oct. 1946.

172. Inactivation of Oestrogens by the Human Liver. [In English.]

By A. WESTMAN. *Gynaecologia, Basel*, **122**, 220–223, Oct. 1946. 2 figs., 6 refs.

After reviewing briefly the literature concerning the inactivation of oestrogens by the liver of animals, the author describes an attempt to treat metropathia haemorrhagica by conducting venous blood from the ovaries to the liver. Six cases were operated on, flaps of omentum or mesentery being embedded in longitudinal incisions in the ovarian cortex and fixed to the ovaries by sutures. In 2 cases the result was good and regular menstruation was restored, but the possibility of spontaneous regression cannot be excluded. There was no improvement in the other 4 cases and finally a hysterectomy was done. At this second laparotomy it was found that in 2 cases the omental flaps had not become adherent to the ovaries. It is noted that in the 2 cases in which the omental flaps were firmly adherent to the ovaries the urinary oestrogenic output was diminished, while in the 2 cases in which the omental flaps had become loosened the urinary oestrogenic output was not diminished. The author concludes that, although the operation is probably of no value from the therapeutic point of view, it provides evidence that the human liver does inactivate oestrogens.

Nicholas Tereshchenko

173. Studies on the Ovary and the Endometrium in Menstrual Anomalies. (Estudios sobre el ovario, el endometrio y las anomalías menstruales.)

By P. A. GOMEZ HERRERA and J. M. BEDOYA GONZALEZ. *Rev. esp. Obstet. Ginec*, **5**, 71–79, Aug. 1946. 7 figs.

Anatomical changes in the ovary were studied in relation to different states of the endometrium in 98 cases. Changes in the endometrium were classified as follows:

   I. Phase of complete secretion.
   II. Phase of incomplete secretion.
   III. Secretory phase in hypertrophic
        endometrium.

IV. (a) Simple proliferation.
    (b) Proliferation with moderate
        hyperplasia.
    (c) Proliferation with marked hyperplasia.
    (d) Atrophic endometrium.

In all cases in Group I luteal tissue was found in the ovary, explaining the secretory state of the endometrium. In 5 cases a normal corpus luteum was found. In the others there were abnormal corpora lutea, but sufficient progesterone had been produced to cause the secretory phase. In 1 case a haemorrhage luteal cyst the size of a tangerine was present. Various other abnormalities were found, including 5 cases where the ovaries contained follicular cysts. It is concluded that it is possible for the cycle to continue in spite of the existence of follicular cysts and that progesterone secretion persists in haemorrhagic corpora lutea.

In Group II there was always a recent corpus luteum, but in 2 cases the corpus luteum was haemorrhagic. Since complete secretory change can take place with haemorrhagic corpora lutea, secretion of progesterone must have been deficient in these cases. In 1 case the corpus luteum had regressed; in 2 cases, luteinization had taken place in a follicular cyst.

Three cases occurred in Group III. Follicular cysts were found in all, but in each there was also a normal corpus luteum, thus showing that a normal follicle had ruptured, in addition to the follicular cysts, and had caused secretory change in an already hypertrophic endometrium. In 12 out of the 36 cases in Group IV (a) normal follicles in process of maturation were found. In others follicular cysts were demonstrated and in 1 a corpus luteum haematoma. In some these were no cystic or maturing follicles, only many atresic follicles, some cystic corpora albicantia, masses of theca cells, and primordial follicles. It is clear that these structures can form oestrogen in sufficient quantities to cause proliferation of the endometrium; this supports the idea that theca-lutein cells produce oestrogens. In Group IV (b), in 20 out of 26 cases normal follicles with a few follicular cysts were found. In others corpus luteum haematomata or regressive corpora lutea were present. In 1 case in Group IV (c) there was a theca-cell tumour. Small cystic ovaries were found in the majority of cases, but some cases showed masses of theca cells and

others showed luteinization, thus demonstrating that endometrial hyperplasia and lutein tissue can coexist. Of the 2 cases in Group IV (d), 1 had small cystic ovaries and the other had abundant atresic follicles. It may be that the ovaries produced no oestrogens or that the endometrium was incapable of reacting.

[The subject of menstrual abnormalities remains something of a mystery. It is interesting to find luteal and theca-luteal tissue demonstrated in the ovaries of women with abnormal endometrium. This suggests that ideas on the function of the corpus luteum need revision.]

Josephine Barnes

174. **A Case of Acquired Haematocolpos in Adolescence due to Trauma in Early Childhood.** By M. M. KENNEDY. *Med. J. Aust.*, 2, 634–635, Nov. 2, 1946. 5 refs.

A girl of 16 attended with a suprapubic swelling. She had never menstruated and the vagina was found to be completely obstructed ¾ in. (2 cm.) above the hymen by a firm membrane. When this was incised 3½ pints (2 litres) of thick dark blood escaped. After repeated dilatation and a plastic operation a vagina of normal lumen was obtained. Subsequently menstruation started normally. There was a history of a fairly severe perineal injury at the age of 5 years, the child falling astride a chair rung, which was said to have penetrated deeply into the vagina. Several sutures were inserted in hospital.

Whether this was an acquired or congenital haematocolpos was not certain. Cases presenting at this age are nearly all of congenital origin. The lumen of the vagina fails to develop completely, and when menstruation starts blood collects above the obstruction. There is often associated genital hypoplasia. The uterus in this case was of normal adult size but the secondary sex characteristics were immature. The acquired form of haematocolpos usually results from senile vaginitis, the vaginal walls becoming adherent following denudation of their epithelium. Since the patients are past the menopause, symptoms arise only when pathological haemorrhage occurs—for example, from fibrosis uteri or carcinoma. Vaginitis in childhood is an occasional cause of the acquired form. The author has not been able to find a recorded

case due to injury. He gives his reasons for believing that this was an acquired haematocolpos due to trauma.

H. J. Croot

175. **Menorrheal Problems in College Women.**
By N. WINTHER. *Amer. J. Obstet. Gynec.*, **52**, 803–809, Nov. 1946. 3 refs.

176. **Intermenstrual Pain.** [In English.]
By A. WESTMAN. *Gynaecologia, Basel*, **122**, 216–219, Oct. 1946. 4 refs.

177. **Pituitary and Ovarian Dysharmony.** (Le syndrome de dysharmonie hypophyso-ovarienne.)
By M. ALBEAUX-FERNET. *Méd. français, Paris*, **6**, 371–374, Dec. 25, 1946.

178. **A Patient with Severe and Prolonged Functional Uterine Haemorrhages.** (Een patiënte met sterke en langdurige functioneele uterusbloedingen.)
By M. A. VAN BOUWDIJK BASTIAANSE. *Ned. Tijdschr. Geneesk.*, **91**, 54–60, Jan. 11, 1947.

179. **A Psychosomatic Evaluation of the Psychiatric and Endocrinological Factors in the Menopause.**
By M. H. GREENHILL. *South. med. J.*, **93**, 786–793, Oct. 1946. 9 refs.

This paper was read before the Section on Neurology and Psychiatry of the Southern Medical Association, and it is concerned chiefly with the subject of the menopause from the point of view of the psychiatrist. The author dislikes the name " menopause syndrome "—a term which, as generally defined, implies the presence of a psychiatric disorder. He objects to the term because of the many misconceptions associated with it, the chief of which is the belief that, if psychiatric symptoms are discovered in a woman at the time of the menopause, these are directly and primarily related to the menopause. This belief is still widely held; the author produces evidence to show that where psychiatric disorders accompany the menopause careful investigation will almost always yield a history of the previous occurrence of such a condition.

As regards the psychoneuroses the evidence tends to show that these never begin with the menopause. Any woman who has symptoms of an anxiety neurosis, hysteria, phobic state, compulsive-obsessive neurosis, or hypochondriasis in the menopause has had the condition in her earlier

years. In some cases the psycho-neurosis continues through the menopausal period without significant change. In others there is an accentuation of symptoms; the whole concept of the menopause and all that it means may cause psychoneurotic problems to become acute. It may happen that for many years before the menopause the woman has been in excellent health so, that it might be supposed that the psychoneurosis had come into being at the time of the climacteric. In most cases, however, investigation will reveal a history of a psychoneurosis and that a period of remission has been experienced.

Involutional melancholia, characterized by depression, agitation, and paranoid ideas, may be an exception and may originate at the time of the menopause. It is not denied that most women have at least mild feelings of anxiety about undergoing the climacteric. The healthy woman, however, who has no background of psychological disorder will generally overcome her depression doubts and fears without much difficulty.

Oestrogens are seldom effective in the treatment of the " menopausal syndrome ". They have little or no effect on psychoneurotic disorders, and they are to be recommended only in those instances in which autonomic symptoms (tremors, dilated pupils, pallor, or flushing) have existed before the menopause and have been accentuated by it.

T. C. Clare

180. **Hormone Therapy of Postmenopausal Complaints.** (Hormonale Therapie postklimakterischer Beschwerden.)
By A. SAURER. *Schweiz. med. Wschr.*, **76**, 1198–1201, November 23, 1946. 2 figs.

See also No. 98.

Sterility.

181. **Childlessness and the Small Family. A Fertility Survey in Luton.**
By R. M. TITMUS and F. GRUNDY. *Lancet*, **2**, 687–690, November 9, 1946. 3 refs.

In 1945 a social survey was launched in the borough of Luton, which has a population of about 101,000. A report of this survey, with a full description of the method and operation, has appeared as *A Report on Luton* (Luton: Gibbs and Bam-

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forth). This paper gives an analysis of the information obtained by the survey in so far as it concerned fertility. Information was obtained from samples totalling 3,803 married women, and some of the material collected is submitted in the form of tables and analyzed in the present paper. Four main tables are submitted, as follows:

Table I.—Percentage of married women who have not borne at least 1 live child (classified by duration of marriage and in age groups).

Table II.—Percentage of wives aged under 45 having at least 1 or 2 children within the first 5 years of marriage (classified by duration of marriage and in age groups).

Table III.—Distribution of live-born children to wives aged under 45 after a marriage duration of 10 to 15 years.

Table IV.—Size of families. Relative frequency of families of different sizes born to wives married at the age of 20 to 25.

To supplement the survey an analysis was made of the histories of pregnancy of all married women who bore a live child during 1945, a total of 1,961 women being concerned.

In their summary and conclusion the authors make it clear that it would be wrong to assume that what is true of Luton is also true of the rest of the country, because Luton has its own peculiar problems of population and industry. The summary, as given by the authors, of the " more notable biological facts " reported is as follows: (1) There is no evidence of any increase in the proportion of childless marriages over three generations, and (given the same age at marriage) no marked social class differences. (2) The degree of control over childbearing within marriage, hitherto exercised by women marrying in the late twenties and early thirties, is now in process of being adopted by those marrying in earlier ages. (3) For many wives there is now a long interval of time between marriage and the first pregnancy, and between the first and subsequent pregnancies. (4) Only a small proportion—less than 2 per cent —of all wives can now be described as continuously childbearing. (5) A large increase has been noted in the proportion of one-child and two-child families in recent years, and a dramatic fall in the proportion of families containing 5 or more

children. (6) The trend towards a smaller family size continued during the war—despite a rise in the birth and reproduction rate.

R. H. Parry.

182. Simplified Management of Relative Sterility.
By R. Torpin. *J. med. Ass. Georgia*, 35, 285–288, October 1946. 28 refs.

The author says the subject of sterility is often made so complicated by experts that the general practitioner thinks it is out of his province. This is a great pity, because much valuable work can be done by the practitioner, and the object of this article is to draw attention to simple procedures which are of value. The tubal patency test may conveniently be omitted, as it is of doubtful therapeutic value, and it is usually possible by clinical examination to judge whether the Fallopian tubes are likely to be patent or not. In any case, if the tubes are found to be blocked it is doubtful whether surgical procedures are advisable, as these are so seldom successful. The Huhner test, in which post-coital fluid is taken from the cervix, and upper vagina and examined under the microscope, is of value. It is possible with the naked eye—after a little experience—to judge whether the spermatozoa are normal or not. If the spermatozoa are dead or show little motility the test should be repeated after a pre-coital douche with 2.5 per cent solution of bicarbonate of soda. If the spermatozoa are still dead then the patient should be referred to a urologist. A cervical erosion is a common cause of sterility and may be effectively treated by electric cauterization. It is important to determine the time of ovulation so that advice can be given about the fertile period, and also to know that ovulation is occurring. This may be determined either by a daily temperature recording or by an endometrial biopsy. Any malposition of the uterus, such as retroversion, should be corrected and a pessary inserted. Foci of infection, anaemia, and lowered metabolism should be dealt with in both husband and wife. Thyroid extract is often advisable, also a high protein diet. The author also recommends the use of a 2.5 per cent sodium bicarbonate douche to which corn syrup 1.2 per cent may be added with advantage.

L. W. Lauste

183. **The Problem of Sterility Today.**
By M. E. DAVIS. *Amer. Practit., Phila.*, **1**, 1–14, September 1946. 20 figs.

184. **Male Infertility.**
By R. J. DOUGLAS. *Urol. cutan. Rev.*, **50**, 529–531, September 1946. 9 refs.

The male is responsible for barren marriages in 20 per cent to 50 per cent of cases. General male debility due to tuberculosis, nephritis, diabetes mellitus, and syphilis may coexist with marked fertility, while many infertile males give no evidence of ill health. Local conditions are important, such as bilateral epididymitis, urethral stricture, hypospadias, pin-point meatus, bilateral vasectomy, prostatectomy, perurethral bladder-neck resection, old trauma, testicular tuberculosis or atrophy, and bilateral cryptorchidism. Contributory causes include an infantile penis, male impotence, and premature ejaculation.

Semen examination is essential. The condom method is responsible for many errors, and a sterile glass container is the most satisfactory method of collecting the specimen. The normal volume of ejaculate is from 2.5 to 6 ml., 3 ml. being the average and 70,000,000 spermatozoa per ml. the accepted standard. However, Hotchkiss found that 25 per cent of fertile males had a count below 20,000,000, and fertility has been reported with much lower counts. Spermatozoal morphology is very important. When the percentages of abnormal forms is 25 or more infertility is the rule. Clumping of spermatozoa is also usually associated with infertility. Spermatozoal virility is important. Where activity is little impaired after 12 hours marked virility is indicated, and vice versa.

Whereas the use of testosterone in infertility has usually been considered to be contra-indicated, the authors conclude that it is of benefit, being of greatest value in subfertility, especially with normal sperm count but a lack of spermatozoal vigour. Testosterone may be of use in aspermia, and is frequently helpful in coital failure.

Alex E. Roche

185. **Sterility in Males.** (De steriliteit van den man.)
By L. I. SWAAB. *Ned. Tijdschr. Geneesk.*, **90**, 1796–1808, November 30, 1946. 72 refs.

Abnormalities of the Reproductive Organs

186. **Absence of Vagina and Uterus.**
By H. A. RIDLER. *Med. J. Aust.*, **2**, 774, November 30, 1946.

187. **Vesico-Vaginal Fistula.**
By D. M. SATUR. *J. Obstet. Gynaec., Lahore*, **7**, 141–149, September 1946.

Infections of the Reproductive Organs.

188. **A Case of Acute Generalized Gonococcal Peritonitis.** (A propos d'un cas de péritonite aiguë généralisée à gonocoques.)
By R. GUENIN. *Gynaecologia, Basel*, **122**, 224–232, October 1946. 18 refs.

The literature on generalized gonococcal peritonitis (as opposed to a localized inflammation of the pelvic peritoneum) is reviewed. The disease appears to be more frequent in children than in adults; there is, as a rule, no definite evidence of gonorrhoea on simple inspection; the gonococcus invades the peritoneal cavity either through the ostium of the Fallopian tube or by direct spread through the tubal wall. The clinical picture is that of an acute abdominal condition and a correct diagnosis cannot be made unless a vaginal examination is carried out: this will be painful if the peritonitis is gonococcal in origin and painless in the other conditions which give rise to a generalized peritonitis. The prognosis is good. The treatment is laparotomy with drainage and chemotherapy. One illustrative case is described.

Nicholas Tereshchenko

189. **Pelvic Inflammatory Disease. A Survey of 300 Consecutive Cases, with Special Reference to Treatment.**
By J. E. TRITSCH, I. H. SAXE, and E. SCHNEIDER. *New Engl. J. Med.*, **235**, 414–416, September 19, 1946. 5 refs.

Sulphonamides are now established in the treatment of infective conditions. The authors, however, doubt their value for pelvic inflammatory disease and quote others in support of this view. A consecutive series of 297 cases was taken, all with inflammatory disease of the pelvis severe enough to need hospital treatment, some patients being

desperately ill, while 2 died. The age distribution was as follows: 56 per cent were under 25; 30 per cent between 25 and 35; and 14 per cent over 35. All were kept in bed. One group was treated by rest alone, another by rest and sulphanilamide or sulphadiazine, and a third by surgery. The chief complaints were of pelvic pain and vaginal discharge. Operation was performed if pelvic masses persisted.

Improvement was obtained by rest alone in 91 per cent of cases, compared with 89 per cent treated with sulphonamides. Cure resulted in 6 per cent with rest alone and in 6 per cent with rest and sulphonamides. With operation, cure was obtained in 37 per cent, while 63 per cent were improved. The total incidence of surgical intervention was 14 per cent and was progressively lower in the younger age group.

[In the present furore for chemotherapy it is good to see a controlled investigation of this kind. This series is, however, not large; no account is taken of the cause or type of pelvic inflammatory disease, nor is there any mention of how long cases were followed up.]

Josephine Barnes

190. **The Ovary in Salpingitis.** (Estudios sobre el ovario anexítico.)
By A. SOPENA IBANEZ and P. BOTELLA LLUSIA. *Rev. esp. Obstet. Ginec.*, 5, 84–89, August 1946, 8 figs., 5 refs.

Fifty-five ovaries removed from patients with pelvic inflammatory disease were studied macroscopically and microscopically to determine the effect of inflammatory lesions on the ovary and the functional alterations which occur in these cases. It is found that the ovary becomes infected in cases of salpingitis and this infection tends to recurrence and reinfection. Eventually a functional reaction takes place in the ovary. In 62 per cent of the ovaries follicular cysts were present. This was found to lead to anovular menstruation in a high proportion of cases. There was a general tendency to increase the oestrogenic secretion, and this tended to lead to hyperplasia of the endometrium and thus to menorrhagia, metrorrhagia, and polymenorrhoea.

[It is well known that cases of chronic pelvic infection tend to have menstrual disturbances, and this is believed to be due to infection of ovarian tissue, causing functional disturbance of the cycle. This article demonstrates the mechanism of production of these disturbances of function.]

Josephine Barnes

191. **Acute Salpingitis due to Friedlander's Bacillus. Report of a Case.**
By T. W. BOTSFORD and T. D. KINNEY. *New Engl. J. Med.*, 235, 539–541, October 10, 1946. 2 figs., 11 refs.

New Growths of the Reproductive Organs.

192. **The Difficulties of Early Diagnosis of Malignant Tumours of the Female Genital Organs.** (Ueber die Schwierigkeiten bei der Früherkennung maligner Tumoren des weiblichen Genitale.)
By T. RUST. *Gynaecologia, Basel*, 122, 169–184, September 1946.

The difficulties of early diagnosis of malignant tumours of the genital organs in women are discussed and the history of attempts to make the diagnosis sooner is traced. The early symptoms of ovarian carcinoma are described and it is emphasized that abdominal symptoms in a woman should always lead to a gynaecological investigation. In uterine carcinoma the common early symptom is irregular haemorrhage. In all cases a speculum should be passed to inspect the portio vaginalis of the cervix. Colposcopy, introduced by Hinselmann, may be useful. Schiller's iodine test is described and the various findings are tabulated. In cases where the tissues do not stain, or stain inadequately with iodine, a biopsy should be done. Palpation of the internal genital organs should also be carefully carried out, but changes will be found only in advanced cases. The author tabulates the lines of investigation to be followed to exclude early malignant disease. The history of the menstrual cycle and of irregular haemorrhage must be fully investigated. Biopsy of the cervix should be carried out when a raised plaque is found or if an erosion does not respond to treatment. Curettage should be performed in every case of abnormal bleeding, in cases of irregular bleeding in the premenopausal period, and in all cases of post-menopausal bleeding. The diagnostic procedures should be repeated when, in spite of negative histological

evidence, the case remains suspect. Control and follow-up of the patient are essential. All women admitted to hospital should have a gynaecological examination and investigation.

[This paper contains much sound sense and if its recommendations are universally carried out, many tragedies due to late diagnosis of female genital carcinomata would be averted.]

Josephine Barnes

193. **Retroperitoneal Tumours Simulating Genital Tract Neoplasms.**
By W. B. STROMME and H. J. STANDER. *Amer. J. Obstet. Gynec.*, 52, 456–463, September 1946. 5 figs., 12 refs.

Retroperitoneal tumours are rare, difficult to diagnose pre-operatively, and usually mistaken for ovarian or uterine tumours. Tumours of the mesentery and retro-peritoneal tumours are believed by many to arise in the mesenchyme surrounding the primitive coelomic cavity. They may be cystic or solid, benign or malignant. They are derived from: (1) retroperitoneal organs and their " anlagen "; or (2) retroperitoneal connective tissue. A classification is proposed. In 12 years in the Women's Clinic of the New York Hospital retroperitoneal tumour was encountered 12 times in 13,113 gynaecological operations. Details are shown in a table. The diagnosis was made pre-operatively 4 times. Two were cases of retroperitoneal cyst of the Wolffian duct, while 1 was a dermoid cyst, 1 a lipoma, 2 fibromata, 1 a fibrosarcoma, 1 a cystadenoma, 1 an adenocarcinoma and 1 a neurilemmoma. The remaining 2 tumours originated in a tuberculous kidney and a hydronephrotic kidney respectively.

One case is described in detail. A married woman, aged 57, had noticed some abdominal swelling since the birth of her last child 17 years earlier. Three years before her admission to hospital she refused operation on her tumour. So large did it become that she was bedridden for 18 months before consenting to hospital treatment. She had few complaints other than those relevant to the size and weight of the tumour: There was no post-menopausal bleeding. A huge abdominal tumour was present. It gave no fluid thrill. The overlying skin was eroded and infected. The cervix was

healthy. For 3 months she rested in hospital receiving skin medication, blood transfusion, and vitamin therapy. At operation, the pelvic organs with normal bowel were found displaced by a large retroperitoneal tumour extending from the pelvic floor to the diaphragm, and originating in the left abdominal sulcus region. Its overlying peritoneum was entered and the tumour was gradually mobilized by sharp and blunt dissection until it was finally removed. Sulphanilamide (6 g.) was sprinkled in the retroperitoneal space and peritoneal cavity. The operation took 4 hours during which the patient received 1,900 ml. of blood. Her condition did not permit of removal of the excess of abdominal wall, which was closed in layers. A stormy post-operative course followed. The abdominal wall healed by secondary intention. A ventral hernia was repaired 3 months later. The patient was in good health when last seen 2 years and 4 months after operation. The tumour when examined measured 13 × 48 × 58 cm. and weighed 59 pounds (27 kg.) There was no macroscopical or microscopical suggestion of malignancy. Histologically it was a myxofibroma.

Valuable in diagnosis of these tumours is the relative fixation of the tumour on abdominal and pelvic examination. Ascites is absent. History is important only in the exclusion of primary pathology of the lower bowel and uterus. The possibility of retroperitoneal tumour must be kept constantly in mind. If it is suspected, intravenous pyelography may help in showing: (1) disturbance or absence of function when the tumour is of renal origin; and (2) a wide displacement of the ureter, and occasionally also of kidney, by the neighbouring retroperitoneal tumour.

Anthony W. Purdie

194. **Treatment of Cancer of the Vulva with Special Reference to Combined Electrosurgical and Radiological Treatment.** (Zur Therapie des Vulvarcarcinomes, mit besonderer Berückischtigung der kombinierten elektrochirurgischen und radiologischen Behandlung (Methode von Berven.))
By J. H. MULLER. *Gynaecologia, Basel*, 122, 193–215, October 1946. 7 figs., 22 refs.

Carcinoma of the vulva is a disease of old age. It is frequently associated with leukoplakia, kraurosis, and other chronic changes in the vulva, and

is often in an advanced stage by the time the patient seeks treatment. Follow-up of the cases shows that radical treatment of the vulva and of the associated lymphatics is necessary to obtain cure. Local excision is followed by recurrence in a relatively short time. In the majority of cases the growth has ulcerated on the surface and is infected when the patient comes for treatment, which may be surgical, radiological, or a combination of both. In surgical treatment there is an immediate operative mortality of 10 to 15 per cent and a permanent cure rate of 2 to 25 per cent (Taussig reports a cure rate of 58.5 per cent.) The treatment consists of excision of the vulva and bilateral removal of lymph nodes *en bloc* combined with intraperitoneal and extraperitoneal excision of the iliac nodes.

The permanent cure rate of radiological treatment is 12 per cent (Stoeckel). Irradiation of the primary tumour leads to retrogression but often a necrotic area appears on the vulva and later a definite secondary tumour. The permanent cure rate of combined treatment is 29 per cent (Cahen). Cahen treated primary growths by radium needles and the region of the lymph nodes with radium plaques and later performed total vulvectomy with radical excision of the inguinal and iliac nodes on both sides. Later Berven combined electrosurgical excision of the vulva with irradiation of the lymph nodes. His immediate operative mortality was 6 per cent. Since 1929 irradiation has been given by teleradium (3 to 5 g. radium bomb). Surgical excision has been carried out after irradiation if the inguinal glands were enlarged and the general condition of the patient permitted. Berven has treated 177 cases with good results.

During the years 1918-45, 40 cases of carcinoma of the vulva have been treated in the Zürich Clinic, some by operative measures alone, some by irradiation alone and all since 1930 by the combined treatment. Since 1940 the author has treated 10 cases by electro-surgical excision of the vulva and radiotherapy of the lymph nodes. If the primary tumour is large it is irradiated first, as thereby the risk of post-operative complications is reduced. The author uses electrodes of 0.5 to 2 cm. thickness and a diathermy apparatus with a current of 4 to 8 amperes. He has modified Berven's technique slightly. After electro-surgical excision of the outer vulval area he inserts a silk thread through each half of the vulva to be excised, and by traction on the threads is able to expose and to get better access to the inner parts of the vulva. Similarly by insertion of a silk thread in the neighbourhood of the clitoris, he obtains better access to the deeper area in this neighbourhood. There was no post-operative mortality in the 10 cases, though 3 of the patients were over 75. The healing of the wound was satisfactory, but more prolonged in those cases which had had previous X-ray therapy. The irradiation technique consists of fractionated irradiation from 1,000 to 4,000 r (surface dose) to large primary tumours before electro-surgical excision; 3,000 to 4,000 r is applied to both inguinal regions and 1,500 to 2,500 r to exactly symmetrical posterior fields. The field size is 10 × 10 cm. or more; the focal skin distance is 50 to 80 cm. The voltage is 180 kV.; filter 0.5 mm. to 0.85 mm. copper, +2 mm. aluminium; average daily dose 200 r.

Not all the cases receiving this treatment have been followed up for 5 years, so that no statistics can be given. It is interesting to note, however, that with one exception there has been no recurrence, although the follow-up has been from $1\frac{1}{2}$ to $5\frac{1}{2}$ years, and it is well known that recurrence and metastases usually reveal themselves within the first year. These results are definitely superior to those obtained by other therapeutic procedures as shown by the following summary of the 50 cases treated in Zürich since 1918: (1) Operative treatment only—3 cases; 1 patient died of carcinoma, 1 of intercurrent disease, and 1 was alive after 5 years. (2) Irradiation treatment only—7 cases; the 7 patients died of carcinoma. (3) Combined operative and irradiation treatment—15 cases; 11 patients died of carcinoma, 1 of intercurrent disease, 3 were alive after 5 years. (4) Combined electro-surgical and irradiation treatment: (a) 1930–1931, 5 cases; 2 patients died of carcinoma, 1 of intercurrent disease, 2 were alive after 5 years; (b) 1940–1945; 10 cases; 1 patient died of carcinoma, 1 of intercurrent disease, 8 were alive after $1\frac{1}{2}$ to $5\frac{1}{2}$ years—average 3 years.

G. Dodds

195. **The Early Diagnosis of Carcinoma of the Cervix.**
By B. D. Best. *Manitoba med. Rev.*, 27, 14-15, January 1947.

196. **The Diagnosis and Treatment of Carcinoma of the Body of the Uterus.**

By S. G. MOCATTA. *Med. Press*, 216, 396–399, November 27, 1946.

197. **Endometriosis: A Surgical Problem.**

By D. MACLEOD. *Brit. J. Surg.*, 34, 109–116, October 1946. 10 figs., 57 refs.

This is a discussion of that condition in which areas of tissue indistinguishable from uterine mucosa are found in abnormal situations. Such tissue is subject to the cyclical changes induced by active ovarian secretion, but the products of " menstruation " have no outlet and may form tumours or cysts. Endometriomata only occur during the childbearing period of life and disappear after the menopause, whether natural or induced. A discussion of the way in which the mucosa becomes ectopic deals with the possibilities of direct invasion, implantation of cells " spilt " out of the Fallopian tube, metaplasia of serosal epithelium (or even of ovarian follicular epithelium); and lymphatic spread. The conclusion reached is " that endometriomata wherever they occur are the result of the endometrium taking upon itself lymphatic permeation."

The sites in which endometriomata develop are enumerated. The commonest place is the ovary, where chocolate or tarry cysts are often found. Other sites are the peritoneum of the pouch of Douglas, the vaginal vault, the recto-vaginal septum, the perineum, the round ligament (even that part in the groin), the umbilicus, the bladder, a laparotomy scar, the small and large bowel, and, very rarely, the ureter. When the small bowel is affected, the pain, vomiting, distension, and constipation may simulate either appendicitis or intestinal obstruction; sigmoid endometriosis may easily give rise to suspicion of obstruction by a carcinoma, and very occasionally blood is passed per rectum at the menstrual time. Even at operation endometriosis of either small or large intestine may closely resemble malignant disease. The history of attacks of pain coinciding with the menstrual periods may help to differentiate. When the bladder is involved there are cyclical crises of frequency of micturition, dysuria, suprapubic pain, and sometimes haematuria. It is pointed out that in women of about 40 treatment by removal of the ovaries or castration by irradiation is fully justified. In younger women this drastic procedure is only to be considered in extreme cases, for example, when otherwise a removal of the rectum might be necessary. Usually local removal of the affected part should be recommended. The author concludes with an interesting epilogue in which he shows that an endometrioma occupies a pathological position midway between a simple and a malignant growth. Though it is an alien tissue in the part where it grows, it is still under the functional control of the ovary. His last sentence is worth special attention: "Is it too much to hope that further study and research in this problem will bring with it the key to the essential nature of malignancy itself?"

[The article is well illustrated by coloured pictures and deserves the attention of all those interested in surgery of the abdomen.]

Zachary Cope

198. **Ectopic Endometrial Tissue in the Thigh.**

By C. P. SCHLICKE. *J. Amer. med. Ass.*, 132, 445–446, October 26, 1946. 3 figs., 2 refs.

The occurrence of a small tumour containing endometrial tissue in the thigh of a Filipino woman is recorded. The patient, aged 35, married, with 5 children and a normal menstrual history, complained that for 3 years she had suffered from a tender lump on the posterior aspect of the left thigh. The lump had steadily increased in size, but was always more swollen and painful during menstruation. Beyond the presence of a deep seated, hard, tender tumour about the size of a golf ball and a handbreadth below the left gluteal fold, nothing of note was found on physical examination.

At operation, the tumour was found to be stony hard, about 4 cm. in diameter, situated in the deep fascia, and intimately adherent to surrounding structures. It was excised together with a cuff of fascia and fatty tissue. Convalescence was uneventful. On section, the cut surface was seen to be grey and speckled with small brown spots. Microscopical examination showed numerous glandular acini containing blood cells and débris lined with epithelium. The glands and the surrounding stroma resembled those of functioning

endometrium. The presence of heterotopic endometrial tissue in such a location is probably best explained by the entry of endometrial fragments into the blood stream. The variations in the tumour with menstruation suggest a response to endocrine stimulation.

S. S. B. Gilder

199. **Endometriosis. Two Hundred Cases Considered from the Viewpoint of the Practitioner.**

By J. FALLON, J. T. BROSNAN and W. G. MORAN. *New Engl. J. Med.*, 235, 669–673, November 1946. 3 figs., 12 refs.

200. **Cystic Adenomyosis of the Uterus.**

By S. GOLD and P. J. KEARNS. *Amer. J. Obstet. Gynec.*, 52, 840–844, November 1946. 3 figs., 22 refs.

201. **A Review of One Hundred Cases of Ovarian Cancer.**

By E. V. HELSEL. *Amer. J. Obstet. Gynec.*, 52, 435–439, September 1946. 13 refs.

The author reviews 100 cases of ovarian cancer treated from 1929 to 1943. There were 62 papillary cystadeno-carcinomata, 7 pseudomucinous cystadenocarcinomata, 6 granulosa-cell tumours, 8 secondary adenocarcinomata, 5 solid carcinomata, 6 sarcomata of various types, 1 malignant teratoma, 1 leuteoma, 1 Krukenberg tumour, and 3 unclassified tumours. In addition to the ovarian malignancy there were found 11 fibroid uteri, 1 fibroma of the opposite ovary, 12 cases of pelvic infection and 1 of appendicitis, 10 ovarian cysts, 3 pelvic endometriomata, and 1 retained doughnut pessary.

The gross appearance of ovarian cancer is bewildering. An attempt to classify such tumours as solid or cystic is unsatisfactory, as many are mixed. In this series the majority appeared to arise from papillary cystadenomata. Solid primary cancer of the ovary is rare if sarcomata are excluded. As the growth usually spreads by implantation and contiguity distant metastases were found in a small percentage only. At operation about half the patients had ascites. The average age was 47 years, with extremes at 19 and 75 while 63 per cent of the patients were between 40 and 60 years. Menstrual disturbance, mainly metrorrhagia, was present in 29 per cent, while 56 per cent had had a normal menopause. Twenty-four patients were single and 76 married. Only 75 per cent of the married women had borne children, while 18 per cent had aborted. The insidious onset is illustrated by the fact that while 18 per cent were examined within 1 month and 31 per cent within 2 months of appearance of their first symptom, 68 per cent were considered incurable at the first examination. Unfortunately many considered their abdominal enlargement to be due merely to fat. In 65 cases traced, 19 had had an operation plus irradiation, 39 had had operation alone, 2 had had irradiation alone, while 5 had received no treatment. The average survival time was: after operation plus irradiation, 35.3 months; after operation alone, 11.7 months; after irradiation alone, 1.5 months; and after no treatment, 2.5 months.

Histological grading is said to be of little importance in prognosis. All carcinomata primary in the ovary were placed in 3 grades. Grade 1 tumours (least malignant) showed good glandular formation with well differentiated columnar epithelium; a mature type of structure was maintained throughout, except in areas where early malignant changes were going on, such as piling up of epithelium or invasion of the stroma. In Grade II (moderate malignancy), glandular and papillary structures were still present but were poorly differentiated; there were moderate variations in size and shape of cells, nuclear changes, and more extensive invasion. Grade III tumours (most malignant) showed practically solid carcinoma with little evidence of glandular or papillary structure. It is not stated how many tumours were so classified. Study of a small group of patients, all in an unstated age group, gave these inconclusive figures of average survival time: grade I, 37.6 months; grade II, 12 months; grade III, 26.3 months. Clinical grouping is considered of more importance. A group I tumour is completely removable, and there is no gross involvement of any other structure at the time of operation. A group II tumour is completely removable, but shows removable adhesions to or involvement of other structures. A group III tumour is only partly removable because of extension to nearby structures. A group IV tumour is irremovable because of extensive involvement of adjacent parts or distant metastases. Immediate mortality (within 2 weeks of operation) was 17 per cent: 1 (group I), 1 (group II), 11 (group III), and 4 (group IV). This explains why so many

patients received no irradiation. Two tables show survival times ranging from 38 months in group I tumours to 5½ months in group IV tumours. Post-operative irradiation, in general, increases the comfort and improves the psychological state of the patient. It appreciably prolongs the survival time, but its curative value is discouragingly low.

Anthony W. Purdie

202. Carcinoma of the Ovary. (Beitrag zur Klinik und Therapie der Ovarialcarcinome.)
By K. ABT. *Gynaecologia, Basel*, **122**, 140–168, September 1946. 11 figs., 32 refs.

The clinical features, symptomatology, diagnosis, and treatment of 184 cases of carcinoma of the ovary are described and discussed. Diagnosis is not easy, and in many cases errors were made. Only in 21 per cent was a correct diagnosis made by the patient's own doctor. Cysts or tumours of the ovary were diagnosed in 35 per cent, tumours of the uterus in 18 per cent, abdominal tumours in 10.5 per cent. Other patients were referred for menorrhagia or considered to be suffering from colitis, appendicitis, or ectopic gestation. In hospital 34.3 per cent were diagnosed correctly. Care was taken at operation to establish the diagnosis of malignancy, by immediate opening of the specimen and inspection of the opposite appendages, pelvic peritoneum, and lymph-nodes. The distribution of the cases into various groups and the methods of treatment adopted are described. Radical removal of the uterus and appendages was performed as early as possible, and this applied also to cases with metastasis. The results in cases treated by post-operative irradiation were much superior to those where no irradiation was given. About 20 per cent of the patients were cured 5 years after treatment. The author points out that every fifth ovarian tumour is a carcinoma. The diagnosis of malignancy may be difficult and may depend on a careful assessment of clinical and pathological findings.

[This is useful work on a gynaecological problem which often proves distressing. It is hard to feel satisfied with a 5-year cure rate of only 20 per cent in spite of the best treatment. This figure emphasizes the need for early diagnosis and treatment.]

Josephine Barnes

203. Arrhenoblastoma of the Ovary, with a Report of Two Cases.
By G. S. JONES and H. S. EVERETT. *Amer. J. Obstet. Gynec.*, **52**, 614–622, October 1946. 7 figs., 21 refs.

These 2 cases of arrhenoblastoma were studied in the Johns Hopkins Hospital. The first patient, aged 36, was first seen in November 1944, complaining of vaginal spotting every 2 weeks. When 15 years old, she had noticed a fine growth of hair on the upper lip, chin, and cheeks. At the same time her breasts began to develop, and though this development continued normally no menses appeared. At the age of 18 menstruation finally began; the periods were irregular and the flow was scanty and lasted 1 or 2 days. After the patient married at the age of 23 the menstrual interval decreased somewhat and varied from 1 to 3 months, but the amount was unchanged. She never became pregnant though she did not practise contraception. Two months before she was first admitted to hospital slight vaginal bleeding had begun to appear every 2 weeks and a curettage was done in consequence. On examination under anaesthesia it was thought that the uterus contained a small myoma. Microscopical examination of the curettings revealed early proliferative endometrium. The spotting continued at intervals of about 2 weeks until April 1945, when the menses ceased entirely. She was re-admitted to hospital in August 1945, and was then found to be a somewhat obese woman—the obesity being limited to the trunk, the arms and legs being relatively small and muscular. There was hypertrichosis of the cheeks, lips, chin, and chest, masculine distribution of the abdominal and pubic hair, and marked hypertrichosis of the lower back, buttocks, and thighs. The breasts were well developed and pendulous in type. Blood-pressure was 176/96 mm. Hg. On abdominal examination an ill-defined mass could be felt in the left lower quadrant.

On pelvic examination the labia majora were found to be small and the labia minora almost absent. The clitoris was not enlarged. The body of the uterus was small and a mass was found in the right adnexal region. At operation the uterus, Fallopian tubes, and left ovary appeared normal. The right ovary was replaced by a solid tumour 9 cm. in diameter with a purplish-brown corru-

gated surface. There was no evidence of metastases. Total hysterectomy was performed, both Fallopian tubes and ovaries being removed.

Pathological examination showed a normal uterus and patent Fallopian tubes. The right ovary was replaced by the tumour, which was apparently solid and well encapsulated with a smooth surface. It was yellowish-grey in colour and on section had a rubbery consistency and was separated into lobules by white fibrous tissue. Microscopically the tumour was composed almost entirely of well-differentiated tubular elements with very few interstitial cells. The authors consider that the tumour was an arrhenoblastoma with relatively slight masculinizing tendency. The presence of sex abnormalities since puberty might indicate a congenital abnormality of the sex ridge with much later tumour formation. It would seem that the paucity of masculinizing symptoms is related to the scarcity of the interstitial cells of the tumour. This fact has been found to be generally true of the Pick type of tumours.

The second patient, aged 26, first seen in December 1944, complained of menstrual irregularity of 3 years' duration. Menses had started at 12, and until the start of the present trouble had been regular and painless with average loss. She had been married 2½ years but had not become pregnant. When first seen she had had 5 months' amenorrhoea; immediately before that there had been 10 months' amenorrhoea followed by 3 months in which periods were regular and normal. It was noticed at the first examination that the patient's voice was slightly husky and that there was some hirsutism on face, arms and legs, while the pubic hair extended to the umbilicus. The breasts appeared normal. The clitoris was enlarged—2 cm. long by 1.5 cm. in diameter. There was bleeding; the uterus was normal in size and position; the left ovary was normal, but the right was about 2½ times the normal size, firm, and freely movable. A primary determination on a 48-hour specimen showed no pregnandiol. Examination for 17-ketosteroids in two 24-hour urine specimens showed 56 and 36 mg. per 24 hours. Operation on January 2, 1945, revealed a normal uterus and Fallopian tubes. The left ovary was slightly smaller than normal and adherent to the posterior surface of the broad ligament. The right ovary was converted into a small spherical tumour

about 5 cm. in diameter, also bound to the posterior surface of the broad ligament by filmy adhesions. A right salpingo-oöphorectomy was done.

On section the tumour was found to be solid, well-encapsulated, and of soft consistency with a mottled surface of yellow and reddish areas. Microscopically, it was composed almost entirely of interstitial cell elements, large masses of cells with eosin-staining cytoplasm and small hyperchromatic nuclei. These cell masses were interspersed with areas of small spindle cells, which in certain parts could be seen to differentiate into tubular-like structures. Because of the relatively poor development of the tubular elements in the tumour, it was classified as an arrhenoblastoma of the intermediate cell type. Twelve days after operation, the 17-ketosteroid level had fallen to 11 mg. in 24 hours. When last seen, on October 31, menstruation was normal and regular at intervals of 22 to 27 days, and lasting for 4 days. The clitoris was now only 1 cm. long and of 0.7 cm. diameter, but there was no improvement in the hirsutism or voice.

The question of the malignancy of arrhenoblastomata is discussed by the authors. Only about 65 cases have been reported up to date, and in many the follow-up studies are unsatisfactory. The majority of cases appear to be benign, so that a simple oöphorectomy seems advisable, especially as many of the tumours are in young women.

F. J. Browne

204. **Granulosa-Cell Tumour of the Ovary.**
By J. J. BIANCO and G. O. FAVORITE. *Amer. J. Obstet. Gynec.*, 52, 677–680, October 1946. 2 figs., 11 refs.

The literature reveals but a few cases of granulosa-cell tumour in which the diagnosis was made pre-operatively. Half the cases occur during child-bearing age, 5 to 10 per cent before puberty, and the rest after the menopause. In children the symptoms are mainly those of precocious menstruation and somatic development. Amenorrhoea, menorrhagia, or metrorrhagia may be met with during the child-bearing period and after the menopause, but cyclic bleeding is the most common symptom. According to Dockerty, amenorrhea may

be the first symptom. Oestrogens are present in excess in blood and tumour tissue, and this excess is the cause of the symptoms.

The naked eye appearances of the tumour vary considerably. The diameter may be a few milli-metres or it may be large enough to fill the abdomen. On section it may be solid or cystic and it is often associated with cysts of the ovary. The yellowish colour of the cut surface is characteristic and helps to distinguish it. In 10 per cent of cases the tumour is bilateral. The histological appearances are also varied, folliculoid, cylindromatous, pseudo-adenomatous, and parenchymatous types being described. In the authors' case a woman, aged 55, 2-para, began to have climacteric symptoms in 1942. In May 1944, the periods ceased, but in February 1945, after 9 months' amenorrhoea, intermittent vaginal bleeding set in with soreness of the breasts, a tender abdominal swelling, and other symptoms suggesting pregnancy. In March 1945, while lying on her abdomen and reaching for a toy under the sofa, she had a sudden severe pain in the right upper quadrant of the abdomen and right shoulder. On examination a cystic semi-solid tumour the size of an orange was found in the left appendage. From the history and examination the diagnosis of granulosa-cell tumour was made. At operation the abdominal cavity was found to contain about 2 litres of serosanguineous fluid, the origin of which was apparently a large collapsed cyst, which was attached to a multilocular mass in the left appendage. The uterus and the tubo-ovarian mass were removed, the right ovary having been removed when the patient was 17 years old. The tumour was partly solid and partly cystic, the solid portion being intensely yellow. Microscopical examination revealed a granulosa-cell tumour of the cylindromatous type with hyperchromatic nuclei but few mitoses. Sections from the wall of the collapsed cyst showed a wide zone of granulosa cells of similar pattern. The myometrium pre-sented no distinctive features. The endometrial picture is described as " compatible with that described by others in connection with granulosa-cell tumours ", but no further details are given. The patient was alive and well 1 year after operation.

F. J. Browne

205. Post-menopausal Haemorrhage and Malignant Tumours of the Ovary. (Metrorragie postclimateriche e tumori maligni dell'ovaio. La metrorragia come sintoma precoce.)

By G. Niosi-Cuismano. *Riv. ital. Ginec.*, 28, 264–300, July-December, 1945. 9 figs., 57 refs.

Post-menopausal haemorrhage is defined as haemorrhage occurring after amenorrhoea for at least a year in the period when the menopause usually occurs and when general signs of the meno-pause have been present. The literature shows that post-menopausal haemorrhage is an early sign of ovarian carcinoma and that its source is hyper-plastic endometrium. The cause of the hyperplasia is probably folliculin, produced by stimuli from the affected ovary, and perhaps acting indirectly through the pituitary.

Three cases of post-menopausal haemorrhage are reported, the patients having passed the menopause from 3 to 13 years before its occurrence. In each case the haemorrhage was the earliest sign of an ovarian carcinoma. The histological diagnoses on specimens removed by operation were: (1) cystadenocarcinoma, (2) bilateral papilliferous cystadenocarcinoma, and (3) proliferating adeno-cystoma with signs of malignancy. The patient with the third diagnosis later developed an adenocar-cinoma of the corpus uteri, considered to be independent of the ovarian tumour and due to malignant change in the hyperplastic endo-metrium. Since post-menopausal haemorrhage from hyperplastic endometrium is often due to causes other than ovarian carcinomata, immediate laparotomy is not justifiable, but the patient should be frequently examined (say once a fortnight) in case enlargement of the ovary should occur. When operation is indicated the abdominal route is usual, but the vaginal route may sometimes be preferable. A good review of the literature is given.

Raymond Whitehead

206. Ovarian Tumors.

By F. B. Block. *Amer. J. med. Sci.*, 212, 738–754, December 1946. 27 refs.

207. On the Origin of Certain Perisalpingeal Cysts.

By R. A. Reis. *Amer. J. Obstet. Gynec.*, 52, 964–974, December 1946. 12 figs., 8 refs.

208. **Neoplasms of the Broad Ligament.** (Le neoplasie del legamento largo. Rivista sintetico-critica con contributo personale di tre casi.)

By L. NOBILI. *Riv. ital. Ginec.*, **28**, 312–341, July–December 1945. 7 figs., 129 refs.

Benign connective-tissue tumours of the broad ligament are relatively rare, the most frequent type being the fibroma. Primary sarcomata are very rare, and of the recorded cases the diagnosis in 24 (including 3 here described) was certain and in 19 doubtful. Published statistics are discordant, since they include tumours that were not primary and tumours with inadequate histological diagnosis. Primary sarcomata may occur at any age, but are most usual between the ages of 30 and 50 and are slightly commoner on the right side. They vary in size from that of an orange to that of an adult human head; they are usually regular and rounded or oval, with a smooth or finely nodular surface, and firm and elastic. Almost all histological types have been described, including (in order of decreasing frequency) pure sarcoma, fibrosarcoma, chondrosarcoma, myoma sarcomatoides, telangiectatic-haemorrhagic sarcoma, pseudocystic myoma with fibromyosarcomatous degeneration, and fibroreticulosarcoma.

The author's cases consisted of (1) a fibromyxosarcoma diagnosed clinically as an ovarian cyst, (2) a fibroreticulosarcoma (first recorded case) diagnosed clinically as an ovarian tumour, and (3) a fibrosarcoma diagnosed clinically as a solid tumour of the right parametrium. None showed metastases and all were cured by operation. Metastases were noted in 7 of the 24 cases considered certain in the literature; there was no site of predilection. There is no characteristic symptomatology, the best guide to diagnosis being the finding on vaginal examination of a tumour with only slight mobility not connected with the uterus, which is displaced upwards and sideways, with lengthening of the vagina so that the cervix is out of reach of the examiner's finger. The treatmen is early removal of the tumour and if necessary of the uterus and adnexa.

[This is a comprehensive and well-written review.]

Raymond Whitehead

Operations.

209. **Absorbable (Oxidized) Gauze as a Hemostatic Agent in Gynecologic Surgery.**

By W. E. STUDDIFORD. *Amer. J. Obstet. Gynec.*, **52**, 495–499, September 1946. 1 fig., 10 refs.

Fibrin foam, gelatin sponge, and oxidized cellulose have been studied recently as haemostatic agents. With the two former thrombin solution is necessary for haemostasis, but oxidized cellulose is a haemostatic agent in its own right, which makes its use simpler. Kenyon *et al* (*J. Amer. chem. Soc.*, 1942, **64**, 121) found that cellulose in any form—paper, cotton, or gauze—could be oxidized by nitrogen dioxide. By extensive carboxyl formation the original qualities of the material are altered. Shrinkage occurs, some tensile strength is lost, and the material becomes rather yellow. Shrinkage can be minimized by oxidation of the gauze on stretchers. Its most important quality from a surgical point of view lies in its low solubility in a 0.15 molar solution of sodium bicarbonate, the pH of which approximates to that of blood. Its main disadvantage is that it disintegrates in the autoclave and only withstands boiling for 3 minutes. It is sterilized by formaldehyde.

The response of animal tissues to all these forms of oxidised cellulose, and especially to the gauze, has been studied. The gauze has been implanted into a large variety of animal tissues, including parenchymatous organs. It is relatively non-irritating, produces little reaction, and is eventually completely absorbed. The time of absorption depends on the amount of material introduced, the extent of the operative trauma, and the quantity of blood present in the gauze. Oxidized cellulose appears to have a specific affinity for haemoglobin, absorbing it from solution, and forming a chemical combination which turns the gauze brown. In contact with whole blood it rapidly forms a brownish-black gelatinous mass; its bulk increases during this process. These changes account for its haemostatic qualities. It will control free bleeding from experimental lacerations of liver, kidney, and spleen. The implanted material goes slowly into solution and is excreted from the blood stream mainly by the kidneys. Some of the material is carried away by phagocytes not as particulate matter but in solution, causing intense basophilic

staining of their cytoplasm. Its passage does not appear to cause any significant kidney damage. In serous and synovial cavities thin-walled non-inflammatory cysts may form about the gauze. These probably eventually disappear.

The author reports its application in 30 cases to control haemorrhage from various sites. In 15 abdominal operations absorbable gauze was used to control bleeding from raw surfaces: (1) of pelvic peritoneum after removal of adherent adnexal masses (9 cases); (2) in retroperitoneal bleeding (4 cases); (3) in secondary abdominal pregnancy after accidental attachment of the placental margin (1 case); and (4) in oozing from a stitched myomectomy wound (1 case). Two deaths, in no way attributable to the use of absorbable gauze, occurred. It was also used in 15 vaginal operations as follows:

1. To control bleeding at operation (7 cases). This comprised: (a) Oozing at the end of a plastic operation in 4 cases of which 2 were successful and 2 were failures; in the latter, plain gauze should have been placed on top of the absorbable gauze to effect pressure. (b) Profuse bleeding during dissection of prevesical fascia in a plastic operation (1 case). Absorbable gauze was packed against the bleeding area and bleeding stopped. Fascia was united in the midline and the vaginal wall was closed over it. Convalescence was uneventful, and healing perfect. (c) Bleeding from the crater of a carcinomatous cervix (1 case), and from a biopsy wound difficult to suture (1 case) was promptly stopped by application of absorbable gauze with superimposed vaginal packing.

2. To control secondary haemorrhage from the vagina in: (a) Three cases after vaginal plastic operations where haemorrhage was due to disruption of the vaginal vault. Under anaesthesia one or more squares of absorbable gauze were placed against the bleeding areas and the gauze was supported by plain packing. The absorbable gauze was discharged as brownish particles over the next 7 to 10 days. The efficacy of these repairs was in no way adversely affected. (b) Three cases of serious haemorrhage from a disrupted vaginal vault after total abdominal hysterectomy; the results were equally good with this treatment. (c) Haemorrhage on the third day after cauterization of a cervix (1 case), and on the seventh post-operative day after

a biopsy of cervix (1 case). The haemorrhage was in each case similarly controlled.

Absorbable gauze in no sense replaces careful control of haemorrhage by clamp and ligature. Haemorrhage from raw oozing areas is best controlled by applications of absorbable gauze followed by momentary digital pressure. In a few cases it has to be held in position by ordinary packing. This latter can be removed without fear of recurrence. It appears to be harmless even when used in closed cavities.

Anthony W. Purdie

210. **A New Method of Preventing Tubal Occlusion following Operations for Sterility. [In English.]** By A. WESTMAN. *Gynaecologia, Basel,* 122, 133–139, September 1946. 3 figs., 5 refs.

Results of operations to relieve occlusion of the Fallopian tubes are not encouraging. The reasons for failure are a flare-up of inflammation of the tubes after operation resulting in adhesions and damage to the muscular walls of the tubes; there is also the fact that the newly formed ostium tends to grow together after operation. The author describes a new method of salpingostomy in which a plug of cholesterol oxalate, a substance normally present in the adrenals, is inserted into the new abdominal ostium. This substance has a melting-point between 39° and 40°C., is non-irritating, and is easily absorbed. The plugs were at first melted after operation by means of short-wave diathermy, but later it was found that the intravenous injection of 1 to 1.5 ml. of a vaccine of *Bacillus aerogenes faecalis*, previously sterilized with formol, gave better results. The body temperature rose to 40°C. and remained there for a few hours. The time of melting was at first 7 to 14 days after operation, but inflammation occurred despite penicillin therapy. Melting is now performed 1 month or more after operation, and when the plug has been melted the tubes are washed out with penicillin solution while penicillin is also given intramuscularly. It is not possible to give long-term results, but judging by present achievements it would seem that this method is an improvement on older ones. In 51 cases operated on 35 showed a communication between the tube and the abdominal cavity, but the results as regards the occurrence of pregnancy cannot as yet be assessed.

[This may prove to be a useful method of dealing with a difficult problem, though the technique seems very elaborate and the incidence of inflammatory reactions high. Long-term results must be awaited before this can claim to be an improvement on older methods.]

Josephine Barnes

211. **Ligamentopexy.** (La ligamentopexie croisée.) By E. NEGRE. *Presse méd.*, 54, 757, November 9, 1946. 2 figs.

After ventrosuspension by the method of Doleris there is a risk of incarceration of the small intestine, and the object of the author's technique is to avoid this. In his operation the round ligaments are detached and crossed over each other. The distal ends are sutured to the parietal peritoneum, thus obliterating the lateral peritoneal pouch. It is claimed that this procedure eliminates all danger of intestinal occlusion by forming a pelvic diaphragm at the level of the uterus, while maintaining the necessary uterine mobility to allow of enlargement in pregnancy. It also eliminates all possibility of incarceration of the Fallopian tube, as well as the risk of formation of adhesions between the round ligaments and the peritoneum, thus avoiding possible trouble in menstruation and pregnancy, and urinary difficulties and infection.

[This is another addition to the already numerous operations for retroversion. It seems a reasonable procedure, though in the absence of case records of operative results no assessment of the value of this new technique can be made.]

Josephine Barnes

212. **A Modification of Alexander-Adams Operative Technique.** [In English.] By A. M. Ritala. *Acta Obstet. Gynec. scand.*, 26, 598–603, 1946. 10 figs., 11 refs.
See also No. 132.

Urology.

213. **Unrecognized Vesical-neck Obstruction in Women.** By C. E. JACOBSON. *New Engl. J. Med.*, 235, 645–648, October 31, 1946. 3 figs., 6 refs.

With the object of drawing attention to vesical-neck obstruction again and urging early treatment the author presents 3 cases in women. The author summarizes the condition by saying that it occurs in elderly women and appears to correspond to the " *prostatisme sans prostate* " of men. The aetiology is unknown, though there are various theories. The symptoms are the same as in men, and consist in difficulty in urination, urgency, diurnal and nocturnal frequency, and sometimes haematuria. Neurological and gynaecological causes of these symptoms should be excluded. The indications of vesical-neck obstruction are the presence of residual urine and trabeculation of the bladder, sometimes with formation of diverticula and sometimes with cystoscopic changes in the bladder neck. While the author advocates its early diagnosis, he also points out that it is almost impossible to recognize in an early stage. The ideal treatment is resection of the vesical neck, but partial resection is often enough. A sphincterotomy or incision of the posterior vesical lip is helpful but of temporary benefit only.

[The cases are not well described, and it is impossible to gain any idea of the effect of treatment. For example, in case 1, it is stated that after operation " residual urine gradually diminished and within 2 weeks all symptoms had subsided ". Such is the entire information given about the later history of this patient who had had urinary symptoms all her life.]

L. W. Lauste

214. **The Disorders of Micturition.** By H. H. SCHLINK. *Med. J. Aust.*, 2, 512–516, October 12, 1946.

This is a discussion of urological disorders commonly seen in gynaecological practice. Each is briefly described, and the section on urinary fistulae is detailed and particularly helpful. Types of inflammation and their sequelae are first discussed and stress is laid on the frequency of urethritis. Abscesses of Skene's glands are an example of periurethral inflammation—a condition which may lead to stricture. Atrophic lesions round the meatus with accompanying urethritis after the menopause are best treated by oestrogens. In dealing with inflammation of the bladder, a warning is given about excluding and treating any associated pelvic inflammation; the converse is

also true. Among secondary infections due to the presence of residual urine resulting from cystocele and prolapse and those associated with chronic cervicitis, trigonitis is not uncommon.

In dealing with carcinoma of the urethra the author advises interstitial radium locally and deep X-ray therapy to the inguinal glands. The prognosis is poor, Crossen's figures showing 11 out of 25 cases alive after 2 years. In dealing with carcinoma of the base of the bladder secondary to growth in the cervix, operative excision should be undertaken—as in endometriosis, in which the lesion has to penetrate peritoneum and bladder wall before reaching the mucosa.

Retention of urine of psychological origin may respond to acetyl β-methyl choline bromide in oral doses of 0.2 g. 3 times a day; other cases require correction of the gynaecological abnormality causing them. In long-standing cases of prolapse pre-operative lavage of the bladder is useful and, where catheterization is prolonged or an indwelling catheter is used, 6 to 12 g. of ammonium or calcium mandelate daily is said to prevent infection, encrustations, and clogging of the catheter. Stress incontinence is really a gynaecological problem, usually curable by colporrhaphy; in many cases a proper union of the levatores ani is needed as a support to the elevated bladder and repaired sphincter.

Urinary fistulae are discussed in the last part of the paper, emphasis being laid in the first place on distinguishing between incontinence due to pin-point fistula of the bladder, to impaired sphincter mechanism, and to uretero-vaginal fistula. A gauze plug in the vagina and instillation of coloured fluid into the bladder will allow of a distinction between the two types of fistula. Treatment should often be preceded by cystoscopy to study details of the problem; indwelling ureteric catheters at operation may be of the greatest value. At least 6 months should be allowed to elapse after the appearance of a fistula or after its attempted repair before a second operation is undertaken. Cases suitable for immediate repair are naturally excluded. The transperitoneal approach is recommended for high fistulae, but the transvesical approach, in the author's view, is always bad. A vaginal cystotomy well above the fistula may be better than post-operative catheter drainage in vesico-urethro-vaginal fistula, but

urethro-vaginal fistulae may be closed over a catheter. The nearer they are to the vesical sphincter the more difficult they are to cure, but bad results are often due to post-operative mismanagement. A case is quoted in which a vulsellum clamped on the anterior lip of the cervix during curettage produced a tear of the bladder, which was repaired later by an approach from below.

Lastly, injury to the ureter is mentioned and reference made to the value of Frecker's instrument in re-implantation of the ureter. All operations for the cure of urinary fistulae should be followed by insertion of an indwelling urethral catheter from 10 to 14 days, and an indwelling uteric catheter may likewise be helpful in dealing with ureteric injuries. In cases where ligation of the ureter has to be carried out, atrophy of the kidney is usual but nephrectomy may not be necessary for a long time.

Guy Blackburn

215. **Disorders of Micturition in the Female.** By A. B. WALKER-SMITH. *Med. J. Aust.*, 2, 516-519, October 12, 1946.

Abacterial cystitis often starts as a mild urethritis but has been known to develop into one of the most distressing of all vesical conditions. In certain instances arsenic has no effect whatever, but some of these patients have responded well to penicillin therapy. Chronic urethritis, likewise, causes much distress and disability and the aetiology is obscure. Half of the cases show a cystitis and trigonitis on cystoscopy, and in others there is a structure at the bladder neck resembling the median prostatic bar in the male. Instillation of 5 per cent argyrol (argent. protein. mitis), urethral dilatation, and in some cases light diathermy to the bladder neck are useful forms of treatment.

Inflammatory stricture is commoner than the traumatic type, and after-dribbling is a more frequent symptom than dysuria. Residual urine is rarely found. Treatment is by gradual dilatation, and the tendency for the stricture to contract is not so pronounced in the female as in the male. The condition, when it occurs in elderly women, is probably due to atrophic changes, but response to treatment is equally satisfactory.

Urethral diverticula are rare but can be demon-

strated by urethrography. Radical excision is the treatment of choice, with an indwelling urethral catheter for 10 days after operation. Prolapse of the urethra is likewise rare and, if reposition and insertion of an indwelling catheter are not efficacious, operation should be undertaken. In this case it is advisable to insert stay-sutures before cutting the prolapse away, as the mucosa may otherwise slide up the urethra and stricture result.

Diathermy is recommended for urethral caruncle, with insertion of a post-operative catheter for 2 to 3 days and subsequent dilatation to prevent stricture. Lastly, brief mention is made of chronic interstitial cystitis and trigonitis, the latter usually being associated with disease in the generative tract.

Guy Blackburn

See also No. 140.

The Relation Between the Results of ABO and Rh Tests and the Clinical Condition of 2,000 Mothers and Infants

BY

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AND

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In the early months of 1944 we planned a blood-group investigation of 2,000 consecutive cases of women booking for delivery at St. Helier County Hospital. It was felt that from such a series information, referable to both baby and mother, could be obtained which would not be forthcoming from a serological study of only those families in which haemolytic disease of the foetus (erythroblastosis foetalis) had occurred. The condition of (*a*) the baby, and (*b*) the mother, was investigated under the following headings.

The Condition of the Baby.

(1) The frequency of haemolytic disease of the foetus or newborn.

(2) The possibility of the association of a normal infant with the presence of anti-Rh or other atypical agglutinins in the mater-nal serum incompatible with the infant's erythrocytes.

(3) The possible relation between "physiological" jaundice and blood-group incompatibilities between the mother and infant.

(4) The possibility of a serological reason for some of the miscarriages and stillbirths usually relegated to the category "cause unknown."

(5) The relation between parity and the above clinical conditions of the infant.

The Condition of the Mother.

(1) The proportion of Rh negative women with Rh positive infants who form Rh antibodies.

(2) The time at which Rh agglutinins are first detectable in the maternal serum during pregnancy.

(3) The possible association of pre-eclamptic toxaemia of pregnancy and eclampsia with a blood-group incompatibility between mother and foetus.

At the time this investigation was started no large unselected series of cases had been reported. Later Broman (1944) reported the results on 914 random mothers and babies. He found 3 cases of haemolytic disease of the foetus among these. In each case the mother was Rh negative, the infant Rh positive and the maternal serum contained Rh antibodies. He did not find anti-Rh agglutinins in the sera of mothers of normal children or of children showing physiological jaundice. He concluded that there was no connexion between the latter condition and icterus gravis. He also investigated toxaemia of the mother in relation to her ABO group and Rh type, but could not find a connexion. Belson (1946) reported that among 300 unselected pregnancies there was 1 proven case of haemolytic disease and 2 cases in which the infant was mildly jaundiced. The mothers of both these latter infants were Rh negative and the serum of one of them contained Rh agglutinins.

Harrison and Meacock (1945) have reported 280 cases which were referred to them for Rh blood-type investigation. Their series included cases where the infant was stillborn, had a congenital abnormality, suffered from haemorrhagic disease of the newborn, or haemolytic disease of the foetus, or died in the neonatal period from conditions other than haemolytic disease of the foetus or where the mother had toxaemia of pregnancy or repeated abortions. They found no connexion between these conditions and Rh incompatibility, except in the case of haemolytic disease of the foetus.

On the other hand, Javert (1942) found that in 16 cases of hydrops foetalis 5 of the mothers had toxaemia of pregnancy.

Schumann and Levine in 1946, reporting a 62 per cent toxaemia-rate in the mothers of infants suffering from erythroblastosis foetalis, stated that it was highest when the infant was hydropic. In a series of 13 cases (7 proved haemolytic disease and 6 probable) Schwartz and Levine (1943) found 9 instances of toxaemia of pregnancy in the mother and they suggested that the toxaemia might be due to foetal blood being agglutinated in the maternal circulation. They felt that further investigation was necessary.

Halbrecht (1944) studied 60 cases in which icterus appeared within 24 hours of birth, but was not associated with other clinical signs. He gave to this form of icterus the name icterus praecox to distinguish it from icterus gravis and physiological icterus. As in 57 of the 60 cases (95 per cent) the infant's red cells were incompatible with the mother's serum according to ABO blood grouping, he concluded that these incompatibilities played some part in the aetiology of icterus praecox. He also found that of 160 cases of jaundice, appearing more than 24 hours after birth (physiological jaundice) only 48 infants (30 per cent) had red cells incompatible with the mother's serum. In a control series of 2,000 unjaundiced infants the incidence of such incompatibility was 26.5 per cent. Wiener (1946), in a series of 42 cases in which jaundice was noted by the clinicians in the first or second day after birth, found that 81 per cent of the infants had red cells which were incompatible with their mothers' sera according to ABO grouping.

TECHNICAL METHODS.

Blood Samples.

Samples of maternal blood were obtained from a superficial vein. Samples of infant's blood were obtained from the cord. A 2 per cent suspension of the red cells from

the clot was used for grouping and Rh typing. The maternal serum free from red cells was examined for antibodies.

ABO Grouping.

This was performed by the tube technique as described by Taylor, Race, Prior, and Ikin (1942) in which both red cells and serum are tested.

Rh Typing.

The technique was essentially similar to that for ABO grouping except that the tubes were incubated at 37°C. and great care was taken in the reading to avoid breaking up the agglutinates (Boorman, Dodd, and Mollison, 1942). In the early stages of the investigation the samples were tested with 4 anti-Rh sera (2 anti-D, 1 anti-D + anti-C and 1 anti-E); later the anti-E was omitted owing to shortage of serum, and for the last part of the series all samples were tested with a single high titre anti-D serum and those which were negative were then retested with sera containing anti-C and anti-E to detect the R′ (Cde) and R″ (cdE) red cells. However, in the tables the 15 R′ and 7 R″ women found are included among the Rh negatives as they are equally capable of forming anti-Rh agglutinins (Anti-D).

Detection of Rh Antibodies.

The serum from each woman was tested at 37°C. against standard red cells of types R_1R_1 (CDe CDe) R_2R_2 (cDE cDE) and rr (cde cde) in order to detect, and differentiate between, the 6 Rh antibodies, i.e., anti-C, anti-D, anti-E, anti-c, anti-d, and anti-e.

Titration of Antibodies.

The technique for titration of antibodies was that in routine use in this laboratory (Boorman, Dodd and Mollison, 1945) in which serial dilutions of the serum are incubated with standard cells. ABO titrations are kept at room temperature and Rh titrations at 37°C. The titre of the serum is expressed as the reciprocal of the greatest dilution causing agglutination (an even distribution of clumps of 3 or more cells was accepted as evidence of agglutination).

Coombs Test.

(a) *Indirect test.* This test was first described by Coombs, Mourant and Race (1945) for the detection of Rh antibodies, especially the incomplete or blocking antibody. The serum to be tested is incubated with standard red cells as for the direct agglutination test. The supernatant serum is then removed and the red cells carefully washed 3 times in a large volume of normal saline. Anti-human-globulin (prepared in a rabbit) is added to the washed cells and the mixture is allowed to stand for at least $\frac{3}{4}$ hour at room temperature. Since the rabbit serum is anti-globulin, a clumping of the red cells indicates that an antibody-globulin has become attached to them.

(b) *Direct Test.* The direct Coombs test is used for the detection of cells sensitized by an antibody *in vivo*. The red cells to be tested are freed from serum by washing 3 times in a large volume of saline. A 2 to 5 per cent suspension in saline is then prepared. One volume of this suspension is incubated at room temperature from $\frac{3}{4}$ hour to 1 hour. A clumping of the cells indicates that they have an antibody attached to them.

After August 1945, therefore, we used these tests in cases in which the clinical diagnosis was in doubt and in which no antibody could be detected by the ordinary iso-agglutination technique to detect any antibodies which might be present in the maternal serum or any sensitization of the infant's red cells.

SEROLOGICAL INVESTIGATIONS

A blood sample was taken from every case, at the first visit to the antenatal clinic: this was usually at about the 12th week of

pregnancy, but in a few instances was much later.

The ABO group and Rh type were determined and the serum examined for atypical antibodies. Where antibodies were present, these were titrated at monthly intervals until the 34th week of pregnancy and then each week until delivery and again at the 10th day of the puerperium. Where the mother was Rh negative and without anti-Rh agglutinins in her serum or, if Rh Positive, gave a history of unexplained miscarriages or stillbirths, samples were tested at the 34th week of pregnancy, at delivery and at the 10th day of the puerperium. All other cases were retested at delivery only. The ABO group and Rh type of the infant were determined from the cord blood and the infant's red cells were tested against the mother's serum at 37°C. to detect any incompatibility.

CLINICAL CRITERIA.

Haemolytic disease of the foetus and newborn. Each case of haemolytic disease was diagnosed by taking into account both clinical and serological findings. The clinical syndromes included under this heading were : —

(1) Hydrops foetalis.

* (2) " Stillbirth " without hydrops, in the absence of any other obvious cause in cases where the mother's serum contained an atypical antibody incompatible with the infant's red cells.

(3) Icterus gravis.

(4) Congenital anaemia of the newborn.

For more detailed diagnostic criteria see Boorman, Dodd and Mollison (1944).

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* In point of fact there was no case in our series fulfilling these criteria although there were 3 cases (see below) in which the infant was stillborn and the mother's serum contained anti-Rh agglutinins, but they are not considered proven cases of haemolytic disease as we were unable to test the infant's erythrocytes.

Physiological Jaundice.

The cases in this group were reported to us by several different observers and therefore we had to adopt definite criteria. These were that the jaundice should be well marked, transient and develop on or after the second day of life. Three cases where the jaundice developed as early as the first day are also included as there were no other clinical or serological indications for the diagnosis of icterus gravis and the jaundice cleared within 10 days of delivery. The ruling that the jaundice should be well marked no doubt accounts for the small number of cases of physiological jaundice found in the series as the very mild cases are thus excluded.

Stillbirths and Miscarriages.

In accordance with the usual practice we have regarded a foetus dying before the 28th week of pregnancy as a "miscarriage" and after the 28th week as a "stillbirth."

Toxaemia of Pregnancy.

We have followed here for purposes of comparison the standard finally adopted in the People's League of Health Experiment (People's League of Health 1942) and have classed as toxaemic those women with albuminuria with or without, but almost invariably with, hypertension and oedema. Those cases in which there was transient mild albuminuria associated with a urinary tract infection were excluded.

SELECTION OF CASES.

We have called this an unselected series but there are obvious fallacies in applying this term to women booking for hospital confinement when shortage of accommodation entails strict assessment of the need for admission to hospital in each case. We were able to accept a high proportion of the primigravidae who applied in early preg-

nancy, but we booked parous women only if they had had previous obstetric difficulty or some associated disease, or if their circumstances made domiciliary delivery impracticable. This last group, however, is reasonably large and to a very great extent balances those accepted for obstetric abnormalities.

A full statistical survey of the material is being made and will be published elsewhere. However, there was no selection in favour of any of the ABO groups or Rh types as the distribution was almost exactly that expected for a random English population (see Tables I and II). The selection in favour of primigravidae was approximately 10 per cent compared with the Registrar General's figures for primigravidae in this area in 1944. The cases were not selected with any regard to their serological picture with the exception of 2 where there was known to be Rh-sensitization due to a previous pregnancy in which the infant was affected with haemolytic disease.

A follow-up was made of 241 of the women who, having attended the antenatal clinic were for various reasons delivered elsewhere. This was to determine whether we were missing any miscarriages and stillbirths because they were not being delivered in the hospital. There were 14 such miscarriages and 7 such stillbirths. This was greater than the proportion found in the 2,000 cases delivered in the hospital and therefore an attempt was made to determine whether they were due to ABO or Rh incompatibilities. Of the 14 women who miscarried, 13 were Rh positive and one Rh negative; this means in all probability that Rh antibodies would not be present in more than 1 of these cases. Nine of the women were group A, 4 were group O, and 1 was group AB; thus it is most likely that in only a few of them there would have been an ABO

incompatibility between mother and foetus. Of the 7 women whose infants were stillborn all were Rh positive and therefore an Rh incompatibility is unlikely; 5 were group A and 2 group O, and therefore it is to be expected that the foetus would have been compatible with the maternal serum in the majority of these cases. We feel that it is unlikely that many of these stillbirths and miscarriages were, in fact, due to either Rh or ABO incompatibilities between mother and foetus.

The Condition of the Baby.

(1) *The frequency of haemolytic disease of the foetus or newborn.*

The percentage occurrence of haemolytic disease of the foetus in the whole series was 0.60 (12 in 2,000) which is higher than that formerly quoted—0.25 by Javert, 1937—and that found by Broman (1944) but is in accord with the estimate of its frequency now held by most of the workers in this field both in England and the United States of America. Moreover there were 7 infants (3 stillborn and 4 diagnosed as physiological jaundice), where there was an atypical antibody in the maternal serum, who might have been more properly diagnosed as suffering from haemolytic disease. The inclusion of these cases would bring the percentage occurrence of the disease to the very high figure of 0.95 per cent.

The distribution of haemolytic disease of the infant among the various ABO groups of the mother was not significant although the incidence was slightly higher where the mother's blood group was A or AB than where the mother was group O or B (Table II). There was, however, a decided preponderance of haemolytic disease of the foetus where the mother was Rh negative (Table I). In only 1 case of haemolytic disease was the mother Rh positive, and there was an agglutinin of the rhesus type anti-c present.

The following are short case notes of the cases of haemolytic disease of the foetus.

201. K. B., aged 33, 4-gravidae, group O, Rh negative. First pregnancy was normal but in the second and third there was foetal death shortly before term. Postmortem examination of the third child had shown erythroblastosis. The 4th pregnancy progressed normally until the 26th week when, after considerable uterine haemorrhage, for

condition but became jaundiced a few hours later. He was transfused with 250 ml. of Rh negative blood during the first day; this raised the haemoglobin to 144 per cent. The following day he became oedematous and showed neck rigidity. Death occurred on the fourth day and postmortem examination confirmed kernicterus.

610. J. P., aged 36, 5-gravidae, group A, Rh negative. The first baby was normal, the second died of " obstructive jaundice " (in 1939). The

TABLE Ia.

Details of Present Child in 2,000 Families Divided According to Rh Type of Mother.

Blood type of mother		Clinical condition of infant					
		Normal	Stillbirth	Miscarriage	Physiological jaundice	Haemolytic disease	Total
Rh negative	Number	292	6	5	22	11	336
	Per cent	86.9	1.8	1.5	6.5	3.3	16.8
Rh positive	Number	1556	14	9	84	1	1664
	Per cent	93.6	0.8	0.5	5.0	0.1	83.2
Total	Number	1848	20	14	106	12	2000
	Per cent	92.4	1.0	0.7	5.3	0.6	100.0

TABLE Ib.

Details of all the Children in 2,000 Families.

Blood type of mother		Clinical condition of infant				
		Normal and physiological jaundice*	Stillbirth	Miscarriage	Haemolytic disease	Total
Rh negative	Number	539	26	63	20	648
	Per cent	83.2	4.0	9.7	3.1	17.4
Rh positive	Number	2738	67	260	1	3066
	Per cent	89.4	2.1	8.5	<0.1	82.6
Total	Number	3277	93	323	21	3714
	Per cent	88.2	2.5	8.7	0.6	100.0

* No attempt was made to assess the number of previous children who had suffered from physiological jaundice as it was felt that the evidence would be unreliable.

which the woman was transfused, she was delivered of a dead foetus showing signs of hydrops foetalis. The foetus was O, Rh positive and the maternal serum contained Rh antibodies, titre 128.

393. D. R., aged 33, 2-gravidae, group A, Rh negative. First pregnancy was normal but the woman received 2 transfusions (Rh type unknown) during the puerperium. Surgical induction was performed at the 39th week of the second pregnancy because of the presence in her serum of and Rh antibody (titre 2). A 6 pounds 10 ounces baby (group O, Rh positive) was delivered in good

third pregnancy resulted in a 3 months' miscarriage. The fourth pregnancy was normal but the baby (A, Rh positive) developed jaundice soon after delivery (see case report below). The antibody-titre was 8 early in the fifth pregnancy and rose to 64 at 37 weeks. The membranes were accordingly ruptured artificially and a few hours later a baby weighing 6 pounds 12 ounces was delivered, pale but lusty (group O, Rh positive). An immediate transfusion of 200 ml. of Rh negative blood was given through the umbilical vein. Jaundice developed within a few hours and the following day twitch-

ing was noticed. Death occurred on the third day, postmortem examination showing extreme kernicterus. The titre of Rh antibodies in the maternal serum rose to 1,000 after delivery.

685. M. P., aged 35, 3-gravidae, group O, Rh negative, had a normal pregnancy followed by an abortion at 24 weeks, the foetus being macerated. The 3rd pregnancy was normal except for a rising titre of Rh antibodies at the 37th week. Surgical

In the fourth week she appeared to be very well but the haemoglobin had fallen to 46 per cent and she was therefore given a transfusion of 200 ml. of Rh negative blood. This raised the haemoglobin level to 84 per cent and thereafter progress was satisfactory. The titre of Rh antibodies in the maternal serum was 256.

1372. M. M., aged 35, 3-gravidae, group A, Rh negative, had had a normal baby followed by an

TABLE IIa.

Details of Present Child in 2,000 Families Divided According to the ABO Group of Mother.

Blood type of mother		Clinical condition of infant					
		Normal	Stillbirth	Miscarriage	Physiological jaundice	Haemolytic disease	Total
O	Number	820	9	6	55	2	892
	Per cent	91.9	1.0	0.7	6.2	0.2	44.6
A	Number	812	9	6	38	8	873
	Per cent	93.0	1.0	0.7	4.4	0.9	43.65
B	Number	155	2		10	1	168
	Per cent	92.2	1.2		6.0	0.6	8.4
AB	Number	61		2	3	1	67
	Per cent	91.0		3.0	4.5	1.5	3.35
Total	Number	1848	20	14	106	13	2000
	Per cent	92.4	1.0	0.7	5.3	0.6	100.0

TABLE IIb.

Details of all the Children in 2,000 Families.

Blood type of mother		Clinical condition of infant				
		Normal and physiological jaundice	Stillbirth	Miscarriage	Haemolytic disease	Total
O	Number	1450	36	139	3	1628
	Per cent	89.1	2.2	8.5	0.2	43.9
A	Number	1430	41	141	15	1627
	Per cent	87.8	2.5	8.7	1.0	43.9
B	Number	292	12	32	1	337
	Per cent	86.8	3.4	9.5	0.3	9.0
AB	Number	105	4	11	2	122
	Per cent	86.0	3.3	9.0	1.7	3.2
Total	Number	3277	93	323	21	3714
	Per cent	88.2	2.5	8.7	0.6	100.0

induction was performed on this account and resulted in a 6 pounds baby (Group O, Rh positive) being delivered slightly asphyxiated after a normal labour. An hour after birth 150 ml. of Rh negative blood was transfused into a saphenous vein. The baby did not become jaundiced and the haemoglobin on the 6th day was 110 per cent. She was discharged with the mother on the 11th day in good condition and was seen weekly by the paediatrician.

early abortion. Pregnancy and labour were normal but the group O, Rh positive baby weighing 7 pounds 5 ounces was seen to be jaundiced 8 hours after birth, when the haemoglobin was 96 per cent. Jerky movements of the limbs were noted on the second day. On the fifth day 150 ml. of Rh negative blood were given as the haemoglobin had fallen to 54 per cent. During the next 10 days the level did not fall below 84 per cent but thereafter there

was a drop to 70 per cent. The baby progressed well with iron. The Rh antibody-titre rose to 1,000 after delivery.

1521. J. P., aged 24, 4-gravidae, group O, Rh negative, had had 3 normal pregnancies. The fourth pregnancy resulted in a living infant weighing 7 pounds (group O, positive) a week after term. He was never jaundiced but became progressively paler until the 12th day when the haemoglobin had fallen to 50 per cent. He was then transfused with 200 ml. of Rh negative blood with satisfactory result, in that 2 weeks later the haemoglobin was 82 per cent. The child was given iron for a considerable time and did well. The titre of anti-Rh agglutinins in the maternal serum was 2.

1573. E. H., aged 32, 4-gravidae, group A, Rh negative. The first infant was normal. The second was stillborn (cause unknown) and the 3rd was diagnosed as a case of marasmus when 3 weeks old and was in hospital for 7 months but eventually did well. The fourth pregnancy was complicated by pyelitis associated with pathological hydronephrosis. Artificial rupture of the membranes was carried out shortly before term. The foetal heart slowed to 90 beats per minute in early labour but the baby, weighing 6 pounds 11 ounces (group A, Rh positive), cried soon after spontaneous delivery. Slight jaundice was noticed at once and the haemoglobin was only 40 per cent. Rh negative blood, 200 ml., was given a few hours later and the following day the haemoglobin was 100 per cent. This level was maintained until the end of the third week when it had fallen to 80 per cent. The child was followed up by the paediatrician and progressed satisfactorily without further treatment. In this case the titre of anti-Rh agglutinins was 2.

1625. E. N., aged 36, 7-gravida, group AB, Rh negative. This woman's first pregnancy ended by miscarriage: the second produced a stillborn infant after a breech delivery. She had then 3 normal infants. The sixth pregnancy resulted in a baby dying of kernicterus. At the 37th week of the seventh pregnancy surgical induction for a rising incomplete antibody-titre was performed. The infant, weighing 5 pounds 8 ounces (group A, Rh positive), was satisfactory at birth. However, the Coombs test done on the cord blood was positive. The following day there was a very mild jaundice. The haemoglobin was 118 per cent but there was no erythroblastaemia. The next day the jaundice

was deeper and the child was irritable. Haemoglobin 108 per cent. Death occurred on the fourth day from kernicterus proved by autopsy. There were no complete anti-Rh agglutinins in the maternal serum but a strong incomplete or "blocking" Rh antibody—titre 128 by the Coombs technique.

2005. J. P., aged 32, 7-gravidae, group A, Rh negative, had only 3 living children. The third, fourth, and sixth had died of jaundice within a few days of birth. Labour was induced surgically at 38 weeks for a rise in Rh antibody-titre. The 12 pounds 13 ounces baby (group O, Rh positive) was lusty at birth and did not become jaundiced until the following day. On the third day she became drowsy and had grunting respirations and death took place the next day. The haemoglobin level did not fall below 90 per cent and, therefore, transfusion was not given. Postmortem examination confirmed the diagnosis of kernicterus with erythroblastosis. The titre of the anti-Rh agglutinins in the maternal serum after delivery was 64.

2181. G. Y., aged 33, 4-gravidae, group A, Rh negative, had a normal first pregnancy, followed by an early abortion. The third pregnancy was an ectopic gestation resulting in a tubal mole. Curiously enough, this was removed early in her fourth pregnancy before she had missed a period. A baby weighing 6 pounds 5 ounces (group O, Rh positive) was delivered normally at term in good condition but covered with yellow vernix. The haemoglobin was then 112 per cent but had fallen to 93 per cent on the following day when the baby was deeply jaundiced. A blood transfusion of 200 ml. on the third day raised the haemoglobin level to 118 per cent but the child was obviously ill and the limbs were becoming spastic. Death on the fourth day was due to kernicterus, confirmed by post-mortem examination. The titre of the maternal Rh antibodies was 256 after delivery.

2560. A. A., aged 34, 3-gravidae, group B, Rh negative, had 2 normal children. The third infant, group O, Rh positive, weighing 6 pounds 2 ounces was delivered spontaneously at 38 weeks but showed mild asphyxial signs. Jaundice was first apparent on the third day and never severe. The haemoglobin, however, steadily fell from 114 per cent to 80 per cent from the 5th to the 9th day. A level of 70 to 80 per cent was thereafter main-

tained in hospital and follow-up showed rapid improvement. This was a case where the icterus might well have been regarded as physiological, but, as the maternal serum contained an anti-Rh agglutinin (titre 64), it was diagnosed as a mild case of haemolytic disease of the foetus, especially as the baby's washed cells gave a positive Coombs' reaction.

563. A. M., aged 29, 2-gravidae, group A, Rh positive (R_1R_1 CDe CDe). The first pregnancy and labour were normal but she received a transfusion (Rh type unknown) during the puerperium for anaemia associated with sepsis. The 2nd pregnancy was uneventful and resulted in a 6 pounds 15 ounces infant, delivered normally, at term. The following day he was jaundiced and this became very marked on the third day but the haemoglobin did not fall below 112 per cent and there was no evidence of erythroblastaemia. He was discharged free from jaundice on the 11th day, but subsequently developed mild anaemia. The infant was group A, Rh positive (R_1r or CDe cde) and the mother had anti-c (anti-St or anti-Hr) in her serum (titre 8).

The following are notes on 4 cases of haemolytic disease which occurred in the hospital just prior to the present series.

1. N. M., aged 29, 5-gravidae, group A, Rh negative; had 3 normal children followed by a miscarriage at 2 months. The fifth pregnancy resulted in the premature delivery at 36 weeks of twins, 1 macerated (maturity about 18 weeks) The living twin (A, Rh positive), weight 4 pounds 6 ounces, showed evidence of haemolytic disease and died on the fourth day with marked kernicterus. The titre of the anti-Rh agglutinin in the maternal serum was 64.

2. V. M., aged 28, 4-gravidae, group O, Rh negative. The first infant was normal but the pregnancy was complicated by toxaemia and there was a postpartum haemorrhage. The second and third children were stillborn at term. Labour was induced at the 37th week of the 4th pregnancy because of the presence of anti-Rh agglutinins and the history of stillbirths. A 5 pounds 9½ ounces live child (group A, Rh positive), resulted. She became jaundiced 19 hours after delivery and was transfused on the second day. Death occurred on the fourth day, postmortem examination con-

firming the diagnosis of kernicterus. The titre of the anti-Rh agglutinin in the maternal serum was 8.

3. E. N., aged 35, 6-gravidae, group AB, Rh negative. This was the sixth pregnancy of the woman whose seventh pregnancy is described above (No. 1625). The baby weighed 6 pounds 12 ounces, was group B, Rh positive, and became jaundiced soon after birth, dying on the fourth day with kernicterus. Rh agglutinins titre 2 were present in the maternal serum.

4. J. P., aged 35, 4-gravidae, group A, Rh negative. This was the fourth pregnancy of a woman described above (No. 610). The baby weighed 6 pounds 4 ounces, was delivered spontaneously at the 38th week (group A Rh positive), and became jaundiced soon after birth. She was given 3 transfusions during the next 10 days and was discharged progressing satisfactorily. She was readmitted at 4 weeks in extremis due to umbilical haemorrhage and died in spite of transfusion. The titre of Rh antibodies in the maternal serum rose to 512 after delivery.

Of the 17 infants affected with haemolytic disease of the foetus (12 in the series) 2 were stillborn, 9 died in the neonatal period, and 6 survived. All but 1 of these infants who died in the neonatal period showed evidence of kernicterus. There seems to be no obvious reason why approximately 50 per cent of the affected infants developed kernicterus, but this accounts for the fact that, in spite of supervision and treatment, the percentage of affected infants surviving was only 35 per cent.

(2) *The possibility of the association of a normal infant with the presence of anti-Rh or other atypical agglutinins in the maternal serum incompatible with the infant's erythrocytes.*

Dockeray and Sachs (1944) in investigating the blood of 61 unselected pregnant women found anti-Rh agglutinins in the sera of 3 of them who later bore apparently normal infants. One infant was group O, Rh positive; the other 2 were not typed and may therefore have been Rh negative. A

single case has also been described by Goldbloom and Lubinski (1946) in which they found Rh antibodies in the maternal blood without the infant showing any symptoms of haemolytic disease.

In this series there were 4 women whose sera contained atypical agglutinins but whose infants were apparently normal.

The notes of these 4 cases and of 3 others which were just prior to the series are given below:

753. F. P., aged 22, 1-gravida, group O, Rh negative, had a normal pregnancy and was delivered at term of a child weighing 6 pounds 14 ounces (group O, Rh positive), which progressed normally. The Rh antibodies in the maternal serum rose to a titre of 16.

1458. M. E., aged 46, 5-gravidae, group A, Rh negative, had had 4 normal deliveries at home. The third baby had died jaundiced on the 11th day. The mother had mitral stenosis but went through pregnancy and labour at term without trouble. The baby (group A, Rh positive) appeared to be completely unaffected. The maternal anti-Rh agglutinins never rose above a titre of 2.

1824. K. K., aged 42, 6-gravidae, group O, Rh negative, had had 5 large infants who had progressed normally. Her pregnancy and delivery at term of a 7-pound baby, group O, Rh positive, were uneventful and the baby was unaffected. The anti-Rh agglutinin titre was 4 and there was also an incomplete Rh antibody present, titre 64 by the Coombs' technique.

2229. D. G., aged 28, 6-gravidae, group A, Rh negative, had had a normal child followed by a premature infant which died on the second day. The third child was normal and the fourth pregnancy resulted in a 2 months' abortion. The fifth pregnancy was uneventful but the 8-pounds baby died of jaundice on the second day. We first saw her at the 34th week of the sixth pregnancy. Rh antibodies (titre 8) were detected but weekly specimens did not show any rise in the titre. A high rupture of the membranes was carried out at the 38th week for hydramnios. The baby weighed 6 pounds 7 ounces, made normal progress, and was found to be Rh negative.

5. F., aged 32, 4-gravidae, group A, Rh positive (R_1r or CDe cde) had 2 normal children followed by an early miscarriage. During the fourth pregnancy she was found to have anti-E (anti-R_2) agglutinins in her serum and labour was induced at the 38th week by rupture of the membranes. The 6 pounds 14 ounces baby was group A, R_1R_2 (CDe cDE), but seemed to be completely normal. The anti-E titre of the maternal serum was 8.

6. H., aged 30, 1-gravida, group O, Rh negative. She had mild hypertension but no albuminuria nor oedema.

The 6 pounds 12 ounces baby (group O, Rh positive) was delivered spontaneously at the 38th week and appeared to be completely unaffected. The titre of the anti-Rh agglutinins in the maternal serum was 2.

7. R., aged 36, 3-gravidae, group O, Rh negative, had 2 stillbirths. She was delivered in the 41st week of her third pregnancy of a live infant weighing 10 pounds 6 ounces (group O, Rh positive). The child was unaffected. The titre of Rh antibodies in the maternal serum was 1 before delivery rising to 8 a week after delivery.

Of the 7 clinically normal infants 1 was in fact Rh negative and therefore was compatible with the maternal serum in spite of the presence of anti-Rh agglutinins. In the other 6, however, the maternal serum was incompatible with the infant's erythrocytes; in 5 cases the antibody was anti-Rh type anti-D, and in the other anti-Rh type anti-E. These infants were clinically normal and without the slightest degree of jaundice or anaemia.

(3) *The possible relation between "physiological" jaundice and blood-group incompatibilities between mother and infant.*

Among the 106 cases of physiological jaundice there were 4 in which the mother's serum contained an atypical antibody incompatible with the infant's erythrocytes. In 2 cases this was an anti-Rh agglutinin, in 1 an Rh antibody of the incomplete type, and in the other the atypical antibody was unidentified.

The notes of these cases are as follows:

1011. A. I., aged 33, 4-gravidae, group A, Rh negative, had had 2 early miscarriages followed by a difficult forceps delivery at term of a baby which died on the fourth day, of traumatic cerebral haemorrhage. The post-mortem examination did not reveal any other abnormality but histological investigation was not carried out. A transfusion was given to the mother for chronic anaemia. The fourth pregnancy was normal and there was delivery at term of an 8 pounds 12 ounces baby (group O, Rh positive). The child developed slight jaundice on the 2nd day but this was less on the third day and soon faded completely. The haemoglobin was 122 per cent and the blood film did not show any abnormality. Weak Rh antibodies, titre 2, were present in the maternal serum.

1379. I. P., aged 17, 1-gravida, group A, Rh positive, had a normal pregnancy and a 7 pounds 7 ounces baby (group O, Rh positive), born at term, developed only mild physiological jaundice on the fourth day. A strong atypical antibody, titre 16, was present in the maternal serum. It was more active at 37°C. than in the cold, and did not seem to be connected in any way with the Rh system, nor with the sub-groups of A, with M and N, or with P. Unfortunately the woman was very uncooperative and we were unable to obtain serum to carry out further tests.

2270. M. W., aged 23, 1-gravida, group AB, Rh negative, had a normal pregnancy and labour at term. The 7 pounds 13 ounces baby (group B, Rh positive), developed transient jaundice on the 4th day. The haemoglobin was 124 per cent and progress was satisfactory. The mother's serum contained no anti-Rh agglutinin, only a weak incomplete Rh antibody, titre 2. The infant's red cells gave a negative Coombs test.

2450. M. A., aged 24, 2-gravidae, group A Rh negative, had had a normal first baby. She was induced at the 39th week of the second pregnancy for a rising titre of Rh antibodies. The baby weighed 6 pounds 5 ounces (group A, Rh positive), became slightly jaundiced on the fourth day, but this was fading and the haemoglobin was 100 per cent on the sixth day. The maternal Rh antibody-titre rose to 32 after delivery.

It is possible that in the above 4 cases the jaundice was due to the maternal antibody and that they should more properly be regarded as mild cases of haemolytic disease of the newborn. On the other hand they were clinically indistinguishable from physiological jaundice and there is no reason why this syndrome should not occur in cases where there is an atypical antibody quite independently of the presence of such an antibody.

In 25 instances where the infant was suffering from physiological jaundice the maternal serum contained anti-A or anti-B agglutinins incompatible with the infant's erythrocytes (heterospecific pregnancy). There were 359 cases, of heterospecific pregnancy in the series, so that the percentage showing physiological jaundice in this group is not significantly higher than the 5.25 per cent found for the whole series. However, if the 18 cases in which the jaundice became apparent by the second day after delivery are considered, in 11 there were anti-A and anti-B agglutinins in the maternal serum incompatible with the foetal erythrocytes. Thus this confirms the view of Halbrecht that such incompatibilities play some part in the aetiology of the type of neonatal jaundice named by him icterus praecox.

In the remaining 77 cases of physiological jaundice no serological incompatibilities between mother and infant were detected.

(4) *The possibility of a serological reason for some of the miscarriages and stillbirths usually relegated to the category " cause unknown "*.

There were only 20 stillbirths and 14 miscarriages in the series*

Anti-Rh agglutinins were present in the sera of 4 of the mothers having stillborn

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* Excluding the 2 stillbirths diagnosed as due to haemolytic disease of the foetus and reported above.

children. In 3 the infant was not typed, but was probably Rh positive as the maternal antibodies increased in titre. In the other the infant was Rh negative. Details of these 4 cases are given below:

68. E. W., aged 29, 3-gravidae, group O, Rh negative, had post-partum haemorrhage necessitating transfusion after the second delivery. She developed pre-eclamptic toxaemia at the 30th week of the third pregnancy, the baby dying *in utero* 3 weeks later.

Medical induction of labour resulted in delivery of a 2 pounds 11 ounces macerated foetus at the 35th week. Anti-Rh agglutinins, rising from 0 to a titre of 4 were present in the maternal serum; the foetus was not grouped or Rh-typed.

109. M. C., aged 32, 4-gravidae, group A, Rh negative, had had a normal child followed by an early abortion and then by a stillbirth, cause unknown. The present pregnancy was normal but she was delivered of a macerated foetus at term. The placenta did not show evidence of erythroblastosis. (Notes kindly supplied by Mr. Bruce Dewar.) The foetus was not grouped or Rh-typed. However the foetus was, no doubt, Rh positive as the titre of Rh antibodies in the maternal serum rose from 0 in early pregnancy to 8 after delivery.

1158. M. H., aged 38, 5-gravidae, group O, Rh negative, had had 3 normal children followed by a full-time child delivered at home who died of jaundice on the second day. The 5th pregnancy resulted in a macerated foetus delivered at home at 37 weeks. We had not seen her at the hospital clinic for several weeks and have no details of the maturity when foetal death occurred. A few days after delivery the titre of maternal Rh antibodies was 32.*

2922. H. K., aged 38, 13-gravidae, group A, Rh negative, had 11 living children. The third pregnancy resulted in 1 living and 1 stillborn premature twin and the child of the 4th pregnancy was stillborn (cause unknown). The 13th pregnancy was complicated by mild hypertension and oedema

* The following year labour was induced at the 37th week for rising Rh antibodies. The 6 pounds 14 ounces baby developed icterus gravis but survided after transfusion. This 6th pregnancy is not included in the series.

but albuminuria did not develop. Labour was induced at the 39th week by rupture of the membrane on account of the presence of Rh antibodies but labour did not start until 3 days later following concealed and revealed accidental haemorrhage necessitating transfusion. The 8-pounds baby was stillborn but the foetal heart sounds had been satisfactory until bleeding started. This child was found to be group A, Rh negative, and so the stillbirth was not connected with the presence of anti-Rh agglutinins (titre 2) in the maternal serum.

Of these 4 stillbirths, therefore, 3 may have been due to haemolytic disease of the foetus although in the 1 there was the added complication of toxaemia of pregnancy of the mother. The fourth was apparently due to the accidental haemorrhage. Of the remaining 16, 5 were due to congenital defects, 1 to extreme prematurity, 2 to prolapsed cord, 1 to accidental haemorrhage, 1 to syphilis, 1 to cerebral haemorrhage and marked generalized oedema (this infant was twin to one which died during the neonatal period from cerebral haemorrhage) and in 5 the cause was unknown. It was not possible to type the foetus in every case but in the majority which were typed there was no incompatibility between the maternal serum and the infant's erythrocytes on the ABO system.

There did not seem to be a serological cause for any of the 14 miscarriages for there was no Rh or ABO incompatibility detected between mother and foetus where it was possible to type the foetus, and in no case was there an anti-Rh or other atypical agglutinin, nor an exceptionally potent anti-A or anti-B agglutinin present in the maternal serum in those cases in which it was not possible to type the foetus. These findings would seem to disagree with Levine's hypothesis that miscarriages are often due to heterospecific pregnancy. This is not necessarily so, however, for the number of heterospecific pregnancies (359) in the series is less than the expected number, and as bookings were seldom made

before the 12th week of pregnancy early miscarriages may account for the missing heterospecific pregnancies. (For a full discussion of this point, see Boorman and Dodd, *Annals of Eugenics*, to be published.)

(5) *The relation between parity and the above clinical conditions of the infant.*

Haemolytic disease of the foetus. In the case of haemolytic disease where the mother was Rh positive and the agglutinin anti-c, the affected child was the second in the family. However, the mother had been

women with Rh positive infants which has to be considered. This total includes 11 where the infant was not typed and so may have been Rh positive. In 1 case a second child was affected but here the mother had had 2 transfusions (of blood which had not been Rh typed, but was probably Rh positive), after delivery of the first infant. The incidence of haemolytic disease of the foetus was high after the third pregnancy as is seen from Table III. Some idea can be obtained from this table also, with regard to the probability of Rh negative women with Rh positive husbands

TABLE III.

Clinical Condition of the Infant in Cases Where the Mother was Rh Negative and the Infant Rh Positive (or in a few Cases not Typed).

Place in family		Clinical condition of Infant					
		Normal	Stillbirth	Miscarriage	Physiological jaundice	Haemolytic disease	Total
1	Number	104		3	8		115
	Per cent	90.4		2.6	7.0		54.5
2	Number	47		1	4	1	53
	Per cent	88.6		1.9	7.6	1.9	25.1
3	Number	9	1			4	14
	Per cent	64.3	7.1			28.6	6.6
4 or over	Number	19	2		1	7	29
	Per cent	65.5	6.9		3.5	24.1	13.8
Total	Number	179	3	4	13	12	211
	Per cent	84.8	1.4	1.9	6.2	5.7	100.0

transfused following the birth of her first infant and these transfusions had probably helped to sensitize her.

Of the 336 Rh negative women, 186 were primigravidae and there was no clinical case of haemolytic disease of the foetus among their infants. Moreover, none of the first children of all 336 Rh negative women was apparently affected although there were 11 families in which subsequent children were affected with the disease. As would be expected, there was no case of haemolytic disease of the foetus where the infant was Rh negative and therefore unable to stimulate or react with Rh antibodies. Thus it is the group of 211 negative

having infants affected with haemolytic disease of the foetus, for where the third or subsequent child was Rh positive it was affected with the disease in 28.9 per cent of cases. These families include some where the husband is heterozygous as well as all those where he is homozygous Rh positive. All children of the homozygous husband must be Rh positive, while there is a chance of 50 per cent of the children of heterozygous husbands being Rh negative. In families where the mother is Rh negative and the husband homozygous Rh positive it is likely that the third child or subsequent children will be affected with haemolytic disease; where the husband is

heterozygous Rh positive, however, it may be much later in the family before a child affected with haemolytic disease is born.

Physiological Jaundice.

There was no connexion between parity and the likelihood of the infant to be affected with physiological jaundice (see *Annals of Eugenics,* to be published).

Miscarriages and Stillbirth.

The miscarriage and stillbirth-rate did not alter significantly with parity except that the miscarriage-rate was higher after the sixth pregnancy. This was because the total numbers in the groups 6-para or over were very small, as the fact that in the series there were 2 or 3 women who habitually aborted for various reasons was enough to increase significantly the miscarriage-rate (see *Annals of Eugenics,* to be published).

CONDITION OF THE MOTHER.

(1) *The proportion of Rh negative women with Rh positive infants who form Rh antibodies.*

Of the 336 Rh negative women included in the series, 211 had Rh positive infants. One hundred and fifteen of these were primigravidae, only 1 of whom developed Rh antibodies and then not until the tenth day of the puerperium (the baby in this case was normal). Nineteen of the remaining 96 developed antibodies and 11 of the infants were affected with haemolytic disease of the foetus.

(2) *The time at which Rh agglutinins are first detected in the maternal serum during pregnancy.*

Four of the 24 atypical antibodies found among the 2,000 cases tested were present in the maternal serum early in pregnancy. One of these, titre 2, through pregnancy and puerperium, was in a woman whose

infant proved to be Rh negative and it was no doubt a legacy from her eleventh pregnancy, 4 years previously, when the infant was Rh positive. Two of the others showed a rise in the titre during pregnancy, the titre after delivery rose to 1,000 in each case. In the fourth case the antibody remained at 2 until the 26th week when a macerated foetus was spontaneously delivered, subsequently the titre rose to 128.

Ten Rh negative women who had had no Rh antibodies early in pregnancy were found to have developed them by the 34th week. There was a fairly wide range of titre, from 1 to 64, but 5 out of the 10 had titres of only 1 or 2. In a further 8 antibodies were not detected until delivery and in the 2 remaining not until the 10th day of the puerperium; 1 of the latter was incomplete anti-Rh titre 2 and the other the unidentified antibody, titre 16 (case 1378).

Rh agglutinins are rarely found in the maternal serum early in pregnancy and when present they are often a legacy from the previous pregnancy and so do not indicate whether or not the present foetus is Rh positive. However, should the titre rise during the pregnancy this means that the foetus is likely to be Rh positive and will most probably be affected with haemolytic disease. When antibodies first appeared in the serum late in pregnancy, especially during the last week or so, the infant although Rh positive, is not invariably clinically affected. However, a high titre of atypical antibodies at any period during the pregnancy usually means that the infant will be affected although sometimes only mildly. Now that various tests for the "incomplete" antibody have been devised, both the agglutinin titre and the incomplete antibody titre should be recorded, as both types of antibody may affect the foetus.

In our series we had only 2 cases where the antibody did not appear in the maternal

serum until the tenth day of the puer-
perium; in both cases the woman was a
primigravida and the infant was not
affected.

(3) *The possible association of pre-
eclamptic toxaemia and eclampsia of preg-
nancy with a blood group incompatibility
between mother and foetus.*

There were 93 women who had had
toxaemia of pregnancy, including 2 cases
of mild eclampsia. The distribution of the
ABO groups among these 93 women seems
to be quite normal and therefore there is
no reason for concluding that there was any
connexion between ABO incompatibilities
and toxaemia of pregnancy. Sixteen of the
women were Rh negative, a percentage of
17.2 which is slightly higher than for the
whole series but not significantly so. More-
over, in only 1 case was there an anti-Rh
agglutinin in the maternal serum incom-
patible with the foetal erythrocytes. There
was a connexion between party and toxae-
mia, our findings quite definitely confirm-
ing the known fact that toxaemia of preg-
nancy is most usually associated with a
first pregnancy. Sixty-one of the 93 cases
were primigravidae and if those who had
only had an abortion previously are also
considered as primigravidae there were
70 out of 93. It may be of interest that in
this series the number of primigravidae
(including those having a previous abor-
tion) who had toxaemia of pregnancy was
70 out of 1,223 (5.7 per cent). This is very
close to the percentage (5.4 per cent) found
in the especially fed group of the People's
League of Health experiment, and lower
than that found by them in an untreated
group (7.4 per cent). Ninety of the 93
women having toxaemia of pregnancy had
normal infants; of the 3 remaining, 2 had
" stillbirths " and 1 an infant affected with
physiological jaundice. One of the " still-
births " had a congenital heart lesion, and

the other was Case No. 68, reported above,
where there was added complication of Rh
antibodies in the maternal serum. Thus, in
this series, toxaemia of pregnancy seemed
to have little or no adverse effect on the
baby. This may be due to the fact that we
were fortunate enough to be able to admit
to hospital all women showing early mani-
festations of the disease.

ADDITIONAL OBSERVATIONS.

The Condition of the Baby.

(6) *Neonatal Death.*
There were 26 neonatal deaths in the
series. Five are reported above as due to
haemolytic disease of the foetus with
kernicterus; there were 6 caused by con-
genital defects (see below); 5 by prema-
turity associated with atelectasis; 4 were
due to cerebral haemorrhage; 5 to infec-
tion, and 1 was jaundiced from the second
day, the postmortem findings showing ex-
tensive brain damage, some liver damage
and general congestion, but no evidence of
erythroblastosis.

Apart from the 5 due to haemolytic
disease there was no proved connexion
between the serology of these cases and the
neonatal death of the infant.

(7) *Congenital Defects.*
There were 15 children in the series with
congenital defects. Five were stillborn (4
anencephalic and 1 congenital heart lesion).
Six died in the neonatal period (2 congeni-
tal heart lesions, 2 hydrocephalics, 1
diaphragmatic hernia and 1 oesophageal
atresia). The remaining 4 survived (1
meningomyelocoele, 1 hare-lip, 1 cleft-
palate and 1 meningocoele).

It seems unlikely that these defects had
a serological cause as in no case was an Rh
antibody detected in the maternal serum,
and in only 3 cases was there an incom-
patibility between the mother's serum and

the infant's erythrocytes on the ABO system. However, a large series of congenital abnormalities would have to be investigated before it could be proved how great a proportion of these was connected with serological incompatibilities between the mother and the infant.

(8) *Sex*.

It has been suggested by Halperin, Jacobi and Dubin (1945) that the prognosis for an infant suffering from haemolytic disease is worse if the infant is male. Of the 8 children affected with the disease, reported above, who recovered 5 were male. Here again a larger series would be necessary before any dogmatic statement could be made.

The Condition of the Mother.

(4) *Accidental Haemorrhage*.

Burch (1945) found that among 10 cases of accidental haemorrhage 5 of the women were Rh negative, 3 having anti-Rh agglutinins in their serum. She concluded that while the subject needs further investigation it seemed possible that women with Rh antibodies were exceptionally prone to accidental haemorrhage.

There were only 5 cases in our series showing accidental haemorrhage. Bleeding after the 28th week in the absence of placenta praevia has been classified as accidental haemorrhage. The small number of cases in the series is due to the fact that cases of minor bleeding were, in accordance with the current practice, not designated accidental haemorrhage, but were relegated to the category "cause unknown" without vaginal examination being made for diagnosis of placenta praevia. In 4 of the cases there was no blood group incompatibility between the mother and the infant, although in 1 of them anti-Rh agglutinins were present in the maternal serum, presumably as the

result of iso-immunisation of the mother during a previous pregnancy, as the present infant was Rh negative. In the other case the mother was group B and the baby group A. However, this is far too small a number on which to base any conclusions.

(5) *Previous Stillbirths and Miscarriages*.

Of the 284 families in which there were previous stillbirths or miscarriages there were 119 where the mother was group O, 121 where the mother was group A, 34 where she was group B and 10 where she was group AB. This is not significantly different from the expected blood group distribution. On the other hand there were 56 Rh negative mothers, a percentage of 19.7 per cent, which is higher than for the whole series. This is even more marked when only those families who had more than 1 previous miscarriage or stillbirth are considered, the percentage of Rh negative mothers is then 23.5 approximately. Table IV gives details of the Rh negative families where there was more than 1 previous stillbirth or miscarriage. It will be seen that in 6 there were anti-Rh agglutinins present in the maternal serum, and in 4 the present child was diagnosed as suffering from haemolytic disease of the foetus.

DISCUSSION.

Perhaps the most interesting finding arising from the investigation, and one which can only be discovered from the testing of a large unselected series, is the fact that anti-Rh agglutinins can occur in the maternal serum associated with a normal Rh positive infant. In our series we found 11 such cases (4 of these infants showed a mild transient physiological jaundice). It is possible that in the future a thorough study of similar cases may yield valuable information which may suggest a new approach

to the treatment for haemolytic disease of the foetus.

In view of the possibility of finding a solution to the problem of haemolytic disease we feel that the practice of some form of birth control would be preferable to the sterilization of an Rh negative woman with a history of this disease among her children, especially if she is young. It

for typing sera. Moreover, as with all Rh agglutinating sera, the serologist is absolutely dependent for his supply upon the co-operation of the clinician in persuading the patient to give her blood for this purpose. Until supplies of the rare sera are more plentiful, therefore, it is probably best to reserve them for the genotyping of husbands in families where a case of

TABLE IV.

Details of the Obstetric History of the 17 Rh Negative Women who had more than one Previous Stillbirth or Miscarriage.

No.	Mother's group	Baby's group	Immune antibody	Pregnancies												
				I	2	3	4	5	6	7	8	9	10	11	12	13
201	O neg.	O pos.	Rh	N.	S.B.	S.B.	H.D.									
260	A '	A neg.		N.	Mis.	S.B.	N.	Mis.	N.							
438	A neg.	O neg.		Mis.	Mis.	N.										
676	O neg.	O neg.		N.	Mis.	N.	N.	N.	Mis.	N.	N.	N.	N.	N.		
732	A neg.	O pos.		Mis.	N.	Mis.	N.									
943	O neg.	O pos.		Mis.	Mis.	Mis.	Mis.	N.								
1430	O neg.	B pos.	Anti-B	S.B.	N.	Mis.	N.									
1259	O '	O pos.		Mis.	N.	Mis.	N.									
1451	A '	A pos.		N.	S.B.	N.	S.B.	N.								
1811	B neg.			Mis.	Mis.	S.B.										
1625	AB neg.	A pos.	Rh	Mis.	S.B.	N.	N.	N.	H.D.	H.D.						
2181	A neg.	O pos.	Rh	N.	Mis.	Mis.	H.D.									
2922	A neg.	A neg.	Rh	N.	N.	N.	S.B. Mis.	N.	N.	N.	N.	N.	N.	N.	N.	S.B.
582	O neg.	B pos.	Anti-B	N.	S.B.	Mis.	Mis.	N.								
584	O neg.	A pos.	Anti-A.	Mis.	Mis.	Mis.	N.									
109	A neg.		Rh	N.	Mis.	S.B.	S.B.									
1011	A neg.	O pos.	Rh	Mis.	Mis.	N.	J.									

N. = Normal	Mis. = Miscarriage	S.B. = Stillbirth
H.D. = Haemolytic Disease	J. = Jaundiced	

should also be borne in mind that circumstances might arise in which she might have normal infants by another husband who was Rh negative or Rh positive of the heterozygous type.

Ideally the husbands of all Rh negative women after the first pregnancy should be tested in order to find out whether they are Rh positive and if so whether homozygous or heterozygous. At the moment, however, this is not practicable owing to a shortage of the appropriate sera. Such sera are only very rarely produced and then not always in high enough titre to be suitable

haemolytic disease of the foetus has already occurred and the parents are anxious to have another child if possible.

All Rh negative women who have had more than 1 pregnancy should have their sera tested for Rh antibodies at intervals during pregnancy, especially between the 34th week and term, as it is during this period that these antibodies are most likely to be detectable. Should such an antibody be found the question arises whether or not it is advisable to induce labour. This is ultimately, of course, the responsibility of the clinician but the serological findings can

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give him some help in making the decision. If an antibody is detectable early in pregnancy and does not rise in titre, it is possible that the present foetus is Rh negative and it is a legacy from a previous pregnancy, and therefore there is no reason for induction. Occasionally, however, the antibody titre does not rise even when the foetus is Rh positive. The testing of the father may be helpful for, should he prove to be homozygous Rh positive, the foetus must be Rh positive and liable to be affected with haemolytic disease and so it might be wise to induce early. A rising titre of antibodies from early pregnancy to the 26th or 28th week almost always means that the foetus will be affected with the disease. In this case, induction can be undertaken as soon as the foetus has attained a weight and maturity compatible with life. Should antibodies not appear until very late in pregnancy it is probably best to allow the pregnancy to go to term as there is a possibility that the infant, although Rh positive, may be unaffected (there were 2 cases where the infant was normal and 2 where it showed only mild jaundice in our series) and it is not worth exposing it to the dangers of prematurity unnecessarily.

We have not confirmed Javert's finding that signs of distress in labour are common in the affected babies, and feel that, in the absence of any other indication, Caesarean section should not be undertaken. It does not seem justifiable to subject the mother to this extra risk for the sake of a baby which has a considerable chance of developing kernicterus, even if delivered prematurely and transfused.

SUMMARY.

A serological and clinical survey of 2,000 mothers and their 2,024 infants was made.

The mothers were tested serologically during pregnancy as well as at delivery.

The association of normal infants with a maternal serum containing Rh antibodies incompatible with the foetal erythrocytes was found to be more common than has hitherto been believed.

The possible connexion between various clinical conditions and serological incompatibilities is discussed.

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Studies in Prematurity, Stillbirth and Neonatal Death

Part I. Factors Affecting Birth-weight and Outcome

BY

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Introduction.

In the following studies an attempt is made to evaluate the principal aetiological factors influencing the incidence of prematurity, infant deaths and stillbirths. It is based on the records of 7,599 births in in Simpson Memorial Pavilion, Royal Infirmary, Edinburgh, during the 3 years 1943 to 1945 inclusive.

During the past 15 years a large number of similar studies have been made, particularly in America, with widely divergent conclusions. In a detailed review of the literature on prematurity by Anderson and Lyon (1939), the percentage of premature births attributed by different authors to toxaemia of pregnancy is seen to range from 1.4 per cent (Capper 1928) to 29.9 per cent (Dunham and McAlenney, 1936). The figure for antepartum haemorrhage was found to be 1.5 per cent by Brown (1917) and 18.2 by Cook (1921). Heart disease in the mother was found in 8.3 per cent of cases by Rapisardi (1931) but in only 0.1 per cent by Israel and Kemkes (1927) while premature births attributed to unexplained causes were placed as low as 18.8 per cent by Rapisardi and as high as 76.9 per cent by Israel and Kemkes. The main reason for these gross discrepancies would seem to be as follows:

1. The absence of adequate controls. In many of the studies made on prematurity and infant deaths, no control group of mature healthy infants has been included for comparison. Any abnormality or disease occurring during the mother's pregnancy or delivery is apt to be called the cause of the prematurity or death of the infant, though an equal incidence of such abnormalities might well have been found in a control group if this had been included for comparison.

2. Failure to differentiate between emergency and booked cases. The maternity practice of a hospital can be divided into two main groups:—

(a) "Booked" cases who have made arrangements in advance for confinement in the hospital. In this country in recent years this group has included a high proportion of primiparae, with a small number of multiparae who are admitted because of previous bad obstetrical history or chronic disease, or for social reasons. These mothers have usually received antenatal care.

(b) "Emergency" cases, who are admitted in or shortly before the commencement of labour, because of some complication or other urgent reason.

In any attempt to use hospital patients as a sample from which general conclusions can be drawn applicable to the population as a whole, only booked primiparae should be included.

3. The omission in many studies of all consideration of stillbirths. As McNeil (1942) has stated:—

" It is necessary to place alongside any figures of neonatal mortality the corresponding stillbirths. This is especially important in any international comparison of infant mortality rates. Unless this is done, serious errors in the calculation of infant deaths will be made. Further, the dividing line between stillbirths and neonatal deaths, usually so sharply drawn, is misleading, because the same lethal processes that destroy infant life during birth continue to operate with great power after birth, and indeed are responsible for the majority of neonatal deaths."

4. The adoption by different authors of varying criteria of prematurity and of viability. For instance, in a survey carried out by Tyson (1934) on 4,663 deliveries, the premature infant is taken to be one of between $4\frac{1}{2}$ months gestation and 38 weeks, as estimated presumably from the mother's statements and clinical examination. He excluded from his premature group a number of babies who by the usual criterion of weight would have been included, because they were estimated to be full time. Another American author, writing in the same year (Clifford, 1934); in an analysis of the influence of obstetric factors on the viability of 958 premature infants, defines a " premature " baby as one weighing less than 5 pounds, and places those between 5 pounds and 6 pounds in an " immature " group. At the present time, the definition laid down by the International Medical Committee of the League of Nations on a weight basis has gained general acceptance. This defines a premature infant as being one with a birth-weight of $5\frac{1}{2}$ pounds (2,500 g.) or under. Attempts have been made to define a lower as well as an upper limit for the birth-weight of a

premature baby. In certain surveys infants below 1,500 g. (3 pounds 4.8 ounces) have been considered " non-viable " and excluded from the sample. Peckham (1938) in a series of statistical studies on prematurity from the Johns Hopkins Hospital, omits as " previable " all infants less than 1,500 g. in weight, or 35 cm. in length. Recently the suggestion has been put forward by Henderson (1945) that $2\frac{3}{4}$ pounds (1,250 g.) be taken as the lower limit of viability. Now Dunham and McAlenny (1936), in a study of 5,000 births, found that 35 per cent of babies between 1,000 and 1,499 g. at birth survived their stay in hospital, and 1.2 per cent of those below 1,000 g. To call an infant born alive " previable " appears to be a contradiction in terms, and there seems to be little justification for setting a lower limit to the definition of prematurity when applied to liveborn infants. Where stillbirths are concerned, it is more difficult to draw the line between a premature stillbirth and an abortion. Here both weight and estimated gestation must be taken into account.

PROCEDURE.

During the 3 years 1943 to 1945, nearly 8,000 births occurred in the Simpson Maternity Pavilion, Edinburgh. A special code card was designed, on to which was entered details from the obstetric and infant records of every stillbirth, infant death and premature birth occurring during the period. A random 1-in-10 sample was also taken of mature infants born in the hospital and surviving their discharge, to serve as a control group. In making up totals and calculating rates, the figures for mature surviving infants have where necessary been multiplied by 10 to restore the original proportions. Due allowance has been made for this in the tests of significance used.

The following data were obtained for each case:—

1. General information about the mother, such as age, parity, whether married or single, a history of previous pregnancies, and whether booked or emergency.

2. Social data, including occupation of husband, average weekly income and employment of mother during pregnancy.

3. Information regarding the pregnancy and delivery in question; any complicating illnesses or accidents, length of labour and mode and complications of delivery.

4. Information concerning the baby while in hospital; weight at birth and estimated time of gestation, method of feeding in hospital, any pathological conditions occurring in hospital diagnosed clinically in those who survived.

5. Follow-up of the baby as far as possible from records of the welfare clinic which serves all babies born in this hospital. Data recorded included details of feeding, weight and progress.

6. In all stillbirths and deaths, clinical diagnosis and pathological findings at autopsy.

7. Detailed information regarding income, housing, efficiency of the mother was obtained in a smaller sample by home visiting.

The data recorded on the individual code cards were sorted and analyzed.

Outcome according to birth-weight is considered in this paper, and also the various factors affecting the weight of the infant. The next paper in this series deals with delivery and its hazards, and the third with a detailed analysis of deaths and still-births.

Further papers will consider the effect of social factors on prematurity, and infant wastage, and the progress of babies in hospital and after discharge.

BIRTH-WEIGHT AND OUTCOME.

In this paper an infant is regarded as premature if its birth-weight is not more than 5½ pounds. Table I shows the proportion of premature and of mature infants born to primiparae. During the 3-year period under review, the prematurity-rate amongst all primiparae was 8.6 per cent, including 1.7 per cent of babies weighing 3½ pounds or less. At the other end of the scale, there was 0.3 per cent of infants over 10 pounds in weight, regarded as "post-mature." The remaining 91.1 per cent fell within the weight limits of maturity. These figures refer to a hospital sample, which contains booked and emergency cases, as well as multiple and illegitimate births, in proportions different from their incidence in the general population of first births. The last two columns give the figures for booked married women. The prematurity-rate there shown, 5.9 per cent, most nearly represents that to be expected in the population as a whole for legitimate first pregnancies.

Prematurity-rates: Multiparae.

Since multiparae are not normally admitted to hospital unless there is some special reason, such as complication of pregnancy or delivery, bad obstetrical history, or social difficulties, it is not possible to obtain from hospital cases a rate in any way representative of that in the general population.

Outcome According to Birth-weight: Primiparae.

Table II gives the "outcome"—whether the baby survived, died or was stillborn—for all primiparae in each half-pound weight group. These data are plotted in Fig. 1. The survival rate is seen to rise rapidly with increasing weight up to the 5 pounds 9 ounces to 6 pounds group. It then remains steady at about 97 per cent until

TABLE I.

Distribution of Birth-weights Among First-born Infants.

Birth-weight				All primiparae		Unmarried mothers		Multiple births		Booked legit. single births	
Pounds	Ounces	Pounds	Ounces	Per cent	Cumu-lative	Per cent	Cumu-lative	Per cent	Cumu-lative	Per cent	Cumu-lative
Less than	3	9		1.7	1.7	1.2	1.2	9.8	9.8	1.1	1.1
3	9 to	5	8	6.9	8.6	6.9	8.1	49.9	60.7	4.8	5.9
5	9 to	10	0	91.1	99.7	91.7	99.8	40.3	100.0	93.8	99.7
More than	10	0		0.3	100.0	0.2	100.0			0.3	100.0

TABLE II.

All Primiparae: Outcome According to Birth-weight

Birth-weight				Number of cases	Per cent lived	Per cent died	Per cent stillborn	Per cent stillborn of total wastage
Pounds	Ounces	Pounds	Ounces					
1	1	to 1	8	3	—	—	100.0	52.9
1	9	to 2	0	12	—	50.0	50.0	
2	1	to 2	8	19	—	52.6	47.4	
2	9	to 3	0	21	19.0	42.9	38.1	51.4
3	1	to 3	8	32	43.8	25.0	31.0	
3	9	to 4	0	40	47.5	22.5	30.0	55.3
4	1	to 4	8	69	75.3	11.6	13.1	
4	9	to 5	0	91	80.2	7.7	12.1	59.0
5	1	to 5	8	143	85.3	6.3	8.4	
5	9	to 6	0	332	93.4	3.3	3.3	61.9
6	1	to 6	8	600	96.7	0.8	2.5	
6	9	to 7	0	878	96.8	0.8	2.4	73.9
7	1	to 7	8	838	97.8	0.6	1.6	
7	9	to 8	0	852	98.6	0.4	1.0	79.4
8	1	to 8	8	472	95.4	0.8	3.8	
8	9	to 9	0	357	98.0	0.6	1.4	73.3
9	1	to 9	8	177	96.1	1.1	2.8	
9	9	to 10	0	31	96.8	—	3.2	
10	1	to 12	0	15	66.7	—	33.3	100.0
Total				—	94.2	2.1	3.7	63.7
Total number of cases				4982	4693	105	184	

the "post-mature" group of over 10 pounds is reached. Fig. 2 gives the same information in a different way. Here the percentage of all survivors occurring below the stated weight levels is plotted. Similar curves are plotted for "died" and "still-born." The figure shows that, on the whole, the babies who died tend to be smaller than those stillborn, and these again are smaller than those who survived. Among the sur-

vivors, 6 per cent were premature. The corresponding figures for the stillbirths and the deaths are 44 per cent and 62.9 per cent respectively.

In the smaller weight groups, stillbirths form about 50 per cent of the total wastage. The proportion of stillbirths rises with birth-weight, reaching 80 per cent in the mature group and 100 per cent in post-mature infants. The data for both primi-

parae and multiparae are set out in Fig. 3. The line for the latter is similar to that of the primiparae, but on rather a higher level. This is probably due, entirely or in part, to the older age-composition of the multiparous mothers, since, as shown in a later section, the proportion of stillbirths tends to rise with maternal age.
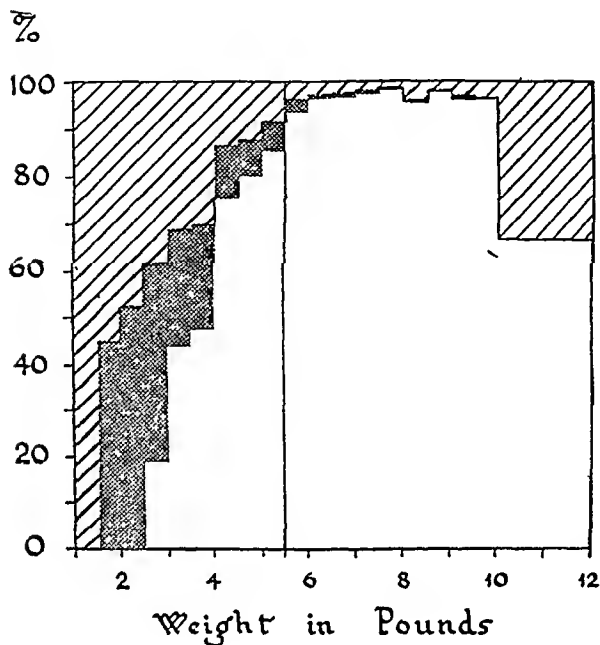
FIG. 1.

Outcome by birth-weight

Shaded—Stillbirths.
Black—Deaths.
White—Lived.
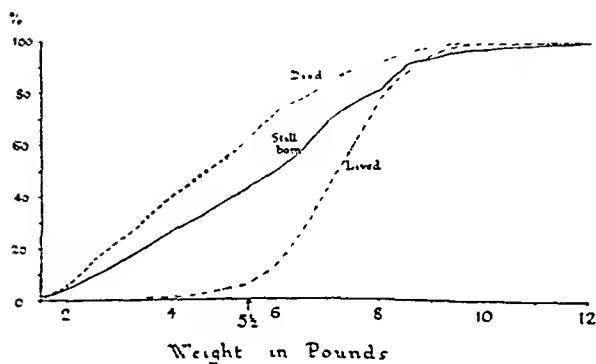
FIG. 2.

Cumulative percentage birth-weight curves.
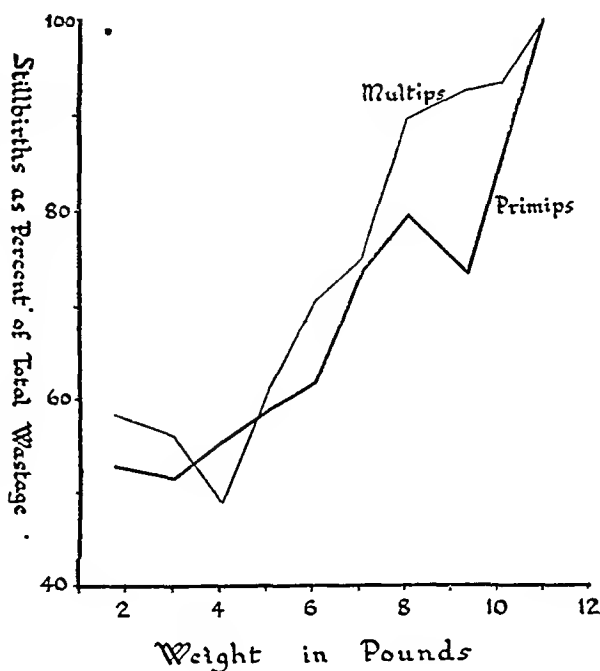
FIG. 3.

Stillbirths as percentage of total wastage.

Outcome According to Birth-weight: Multiparae.

Table III gives the outcome, by weight, for multiparae. This shows a similar picture to that for first births, except that the survival rates at any given birth-weight level tend to be lower. This is what would be expected because of the higher proportion of emergency and complicated cases among the multiparae admitted to hospital.

FACTORS AFFECTING BIRTH-WEIGHT.

1. COMPLICATIONS OF PREGNANCY.

The complications of pregnancy recorded in this investigation fall under three main headings:—

(a) Complications of the pregnancy itself, e.g., toxaemias, pyelitis of pregnancy, hydramnios.

(b) Chronic maternal diseases coincident with the pregnancy, e.g., cardiac disease, syphilis, diabetes.

TABLE III.

All Multiparae: Outcome According to Birth-weight

Birth-weight				Number of cases	Per cent lived	Per cent died	Per cent stillborn	Per cent stillborn of total wastage
Pounds	Ounces	Pounds	Ounces					
1	1	to 1	8	5	—	40.0	60.0 ⎫	
1	9	to 2	0	12	—	33.3	66.7 ⎬	58.5
2	1	to 2	8	24	—	45.8	54.2 ⎭	
2	9	to 3	0	25	8.0	44.0	48.0 ⎫	
3	1	to 3	8	35	22.9	31.4	45.7 ⎬	56.0
3	9	to 4	0	58	50.0	29.3	20.7 ⎭	
4	1	to 4	8	59	66.1	13.6	20.3 ⎫	49.0
4	9	to 5	0	54	72.2	9.3	18.5 ⎭	
5	1	to 5	8	88	81.8	8.0	10.2 ⎫	61.3
5	9	to 6	0	128	85.9	3.9	10.2 ⎭	
6	1	to 6	8	353	93.4	2.0	4.6 ⎫	70.7
6	9	to 7	0	305	95.1	1.3	3.6 ⎫	
7	1	to 7	8	511	95.9	1.0	3.1 ⎭	75.0
7	9	to 8	0	359	97.5	0.3	2.2 ⎫	
8	1	to 8	8	240	95.8	0.4	3.8 ⎭	89.5
8	9	to 9	0	169	94.7	0.6	4.7 ⎫	
9	1	to 9	8	96	93.7	—	6.3 ⎬	94.4
9	9	to 10	0	73	95.9	—	4.1 ⎭	
10	1	to 12	0	23	87.0	—	13.0	100.0
Total				—	89.0	3.8	7.2	65.3
Total number of cases				2617	2329	100	188	

TABLE IV.

All Primiparae: Complications of Pregnancy by Birth-weight

Birth-weight				Number of cases	With complications	Without complications	Per cent with complications
Pounds	Ounces	Pounds	Ounces				
1	1	to 2	8	34	20	14	58.8
2	9	to 3	8	53	33	20	62.3
3	9	to 4	8	109	69	40	63.3
4	9	to 5	8	234	104	130	44.4
5	9	to 6	8	932	344	588	36.9
6	9	to 7	8	1716	358	1358	20.9
7	9	to 8	8	1334	252	1082	18.9
8	9	to 10	0	555	124	431	22.3
10	1	to 12	0	15	2	13	13.3
Total				4982	1306	3676	26.2

(c) Acute illness or injury occurring within 3 months of delivery. "Total complications" comprise all cases falling into any of the above groups.

Total Complications.

Tables IV and V give the total complication-rate in each weight-group for primiparae and for multiparae. These rates are

TABLE V.

All Multiparae: Complications of Pregnancy by Birth-weight

Birth-weight				Number of cases	With complications	Without complications	Per cent with complications
Pounds	Ounces	Pounds	Ounces				
1	1	to 2	8	41	27	14	65.9
2	9	to 3	8	60	46	14	76.7
3	9	to 4	8	117	83 ·	34	70.9
4	9	to 5	8	142	80	62	56.3
5	9	to 6	8	481	207	274	43.0
6	9	to 7	8	816	316	500	38.7
7	9	to 8	8	599	204	395	34.1
8	9	to 10	0	338	115	223	34.0
10	1	to 12	0	23	2	21	8.7
Total				2617	1080	1537	41.3

shown graphically in Fig. 4. The complication-rate falls strikingly with increase in birth-weight. In other words, a mother with a complication of pregnancy is more likely to give birth to a small baby than a woman without complications. Tables VI and VII deal with the same facts in rather a different way. They show, for primiparae and multiparae respectively, the cumulative percentage weight-composition of babies whose mothers had complications, as compared with the no-complication group. It will be seen from Table VI that the prematurity rate for the group with complications (17.3 per cent) is over 3 times that of the group without complications (5.6 per cent), and the percentage of infants of $6\frac{1}{2}$ pounds or under is twice as great

FIG. 4.

Incidence of maternal complications in relation to birth-weight.

TABLE VI.

All Primiparae: Cumulative Percentages by Birth Weights in Cases With and Without Complications of Pregnancy.

Birth-weight		With complications	Without complications
Pounds	Ounces		
Less than:			
2	9	1.5	0.4
3	9	4.1	0.9
4	9	9.3	2.0
5	9	17.3	5.6
6	9	43.6	21.6
7	9	71.1	58.5
8	9	90.4	87.9
10	1	99.9	99.7
12	1	100.0	100.0

when the mother has complications as in the control group. Table VII shows a similar picture for multiparae. Multiple births are excluded from these and subsequent tables where the different criteria of maturity applicable to twins and triplets,

TABLE VII.

All Multiparae: Cumulative Percentages by Birth Weights in Cases With and Without Complications of Pregnancy.

Birth-weight		With complications	Without complications
Pounds	Ounces		
Less than:			
2	9	2.5	0.9
3	9	6.8	1.8
4	9	14.4	4.0
5	9	21.9	8.1
6	9	41.0	25.9
7	9	70.3	58.4
8	9	89.2	84.1
10	1	99.8	98.6
12	1	100.0	100.0

and that complications in the mother tend to lower the birth-weight of their babies. The question arises whether the lower survival-rate in the group with complications is solely due to the increased proportion of smaller babies, or whether there is any adverse effect on the infant of the complication itself apart from that of diminishing its birth-weight. The necessary data are displayed in Tables VIII and IX, which show, for primiparae and multiparae respectively, the survival rates in each birth-weight group for infants born to mothers with and without complications. The survival rates do not appear to be strikingly different in the various weight-groups as when the cases with and without complications are compared, though they tend on the whole to be lower when complications are present.

A more accurate comparison may be

TABLE VIII.

All Primiparae Except Multiple Births: Percentage Surviving by Birth-weights in Cases With and Without Complications of Pregnancy.

Birth-weight				With complications		Without complications	
Pounds	Ounces	Pounds	Ounces	Number of cases	Per cent surviving	Number of cases	Per cent surviving
	Below	2	9	15	0.0	10	0.0
2	9	to 3	8	30	33.3	16	18.8
3	9	to 4	8	49	55.1	28	75.0
4	9	to 5	8	79	78.5	105	81.9
5	9	to 6	8	243	94.7	548	94.9
6	9	to 7	8	338	94.7	1337	98.0
7	9	to 8	8	242	95.0	1082	98.0
8	9 and over			126	95.2	444	96.8

or other features of multiple births, would appear to affect the conclusions to be drawn.

The crude survival-rate in the group with complications is lower than in the controls. It has already been shown that chances of survival increase markedly with every half-pound rise in birth-weight,

made be made by calculating the number of survivors that would be expected in the group with complications if at each weight-level they had the same chances of survival as those of corresponding weight without complications, and comparing this expected number of survivors with those actually observed. These comparisons,

for primiparae and multiparae respectively, are shown in Tables X and XI. The number of "expected" survivors is calcalculated as follows: Weight group 2 pounds 9 ounces to 3 pounds 8 ounces.

A similar calculation is made at each weight-level. A positive difference in the last column indicates that the group with complications did better than the group without complications at that weight-level;

TABLE IX.

All Multiparae Except Multiple Births: Percentage Surviving by Birth-weights in Cases With and Without Complications of Pregnancy.

Birth-weight				With complications		Without complications	
Pounds	Ounces	Pounds	Ounces	Number of cases	Per cent surviving	Number of cases	Per cent surviving
	Below	2	9	23	0.0	12	0.0
2	9 to	3	8	40	20.0	11	18.2
3	9 to	4	8	70	52.9	20	65.6
4	9 to	5	8	68	76.5	44	72.7
5	9 to	6	8	145	82.8	183	92.9
6	9 to	7	8	285	94.7	498	96.4
7	9 to	8	8	204	98.0	395	96.2
8	9 and over			117	94.0	244	94.3

TABLE X.

All Primiparae Except Multiple Births: Observed and "Expected" Survivors by Birth-weights in Cases With Complications of Pregnancy.

Birth-weight				Survival rate, no complications	With complications			Observed minus "expected" survivors
Pounds	Ounces	Pounds	Ounces		Number of cases	Observed survivors	"Expected" survivors	
	Below	2	9	0	15	0	0	0
2	9 to	3	8	0.1875	30	10	5.63	+4.37
3	9 to	4	8	0.7500	49	27	36.75	−9.75
4	9 to	5	8	0.8190	79	62	64.70	−2.70
Total premature					173	99	107.08	−8.08
5	9 to	6	8	0.9489	243	230	230.58	−0.58
6	9 to	7	8	0.9798	338	320	331.17	−11.17
7	9 to	8	8	0.9797	242	230	237.09	−7.09
8	9 and over			0.9685	126	120	122.03	−2.03
Total mature					949	900	920.87	−20.87

Survival-rate without complications
                                    =0.1875.
Number of survivors "expected" in group with complications=number of cases × 0.1875 = 30 × 0.1875 = 5.63
Number of survivors observed = 10
Observed −"expected" survivors = + 4.37

a negative sign indicates that they did worse. The observed and expected survivors were summed for premature and mature infants, and the test of statistical significance described in Appendix A was applied. In all 4 groups—premature and mature primiparae (Table X), and prema-

TABLE XI.

All Multiparae Except Multiple Births: Observed and "Expected" Survivors by Birth-weights in Cases with Complications of Pregnancy.

| Birth-weight | | | | Survival rate, no complications | With complications | | | Observed minus "expected" survivors |
Pounds	Ounces	Pounds	Ounces		Number of cases	Observed survivors	"Expected" survivors	
	Below	2	9	0	23	0	0	0
2	9 to	3	8	0.1818	40	8	7.27	+0.73
3	9 to	4	8	0.6500	70	37	45.50	−8.50
4	9 to	5	8	0.7273	68	52	49.46	+2.54
Total premature					201	97	102.23	−5.23
5	9 to	6	8	0.9290	145	120	134.70	−14.70
6	9 to	7	8	0.9639	285	270	274.71	−4.71
7	9 to	8	8	0.9620	204	200	196.25	+3.75
8	9 and over			0.9426	117	110	110.28	−0.28
Total mature					751	700	715.94	−15.94

ture and mature multiparae (Table XI)—the group with complications did worse than the controls; but the differences are relatively small and statistically not significant. Detailed examination of the tables shows that, at all weight-levels except one, the first-born infants of mothers with complications did worse than the control group. Among multiparae the differences are smaller and more erratic, as would be expected, since the mothers without complications of pregnancy would usually have been admitted because of complication of delivery or some other adverse indication. Tables X and XI therefore suggest, but by no means prove, that complication of pregnancy in the mother may sometimes have a deleterious effect on the baby's chance of survival over and above the effect in depressing the birth-weight. The possibility at once suggests itself that the effect will vary with the nature of the complication. Some kinds of complication may have a big effect on the infant, others none at all. So far all complications have been grouped together. It is now necessary to consider them separately :—

A. *Complication of the Pregnancy Itself.*

The following complications of the pregnancy itself were recorded on the individual code cards :—

1. Pre-eclamptic toxaemia including hypertension. The latter condition was included in this group because the case notes by no means always made it clear whether the condition described was one of pre-eclamptic toxaemia or essential hypertension, especially when the woman was first seen late in pregnancy. In any case, the number of women with hypertension was very small compared with those with toxaemia.

This group was sub-divided into those cases specifically referred to as "mild" and the remainder. A separate class-heading was used for cases having an ante-partum haemorrhage as well as toxaemia.

2. Eclampsia, ante- or intra-partum.

3. Hyperemesis, of sufficient severity to necessitate treatment in hospital.

4. Antepartum haemorrhage, comprising placenta praevia or separation of the placenta from any other cause, except cases associated with toxaemia. It was impos-

sible from the case notes to be certain in every instance whether the antepartum haemorrhage was due to a misplaced placenta or to some other cause. All cases of antepartum haemorrhage have been listed together. Cases of slight bleeding in the latter half of pregnancy, or of prolongation of the menses in early pregnancy, were not included.

5. Pyelitis of pregnancy.
6. Hydramnios.

Table XII shows the proportion of these complications occurring in booked married primiparae, which gives a fair indication of their incidence in the population at large. The percentage among unbooked cases and multiparae is considerably higher, as many of these mothers were admitted because of these complications.

The relation between these complications in primiparae and the birth-weight of the infants is shown in Table XIII. This table gives the cumulative percentages by weight of infants born to mothers having the specified complication. The data in this table are set out in diagrammatic form in Fig. 5. In uncomplicated pregnancies, 0.7 per cent of the infants are $3\frac{1}{2}$ pounds or less,
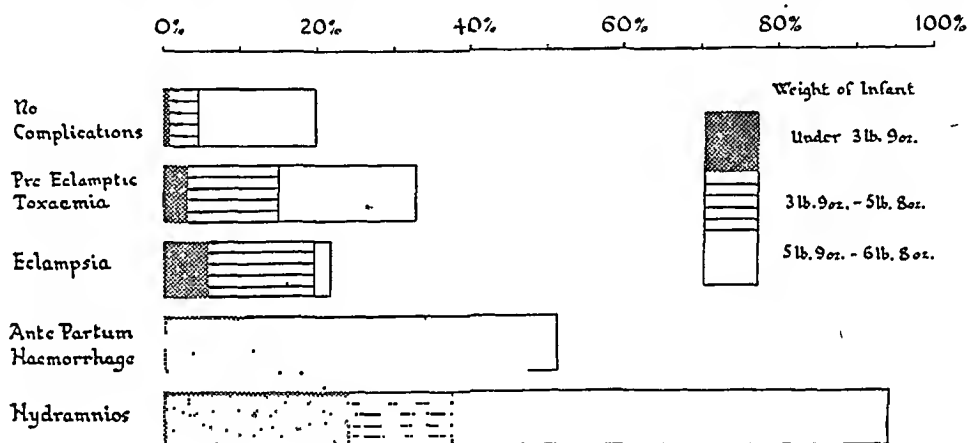
FIG. 5.

Birth-weights in absence and presence of maternal complications.

TABLE XII.

Complications of Pregnancy in Booked Married Primiparae.

Complication	Number of cases	Rate per 100 pregnancies
Pre-eclamptic toxaemia	532	14.0
Mild	232	6.1
Moderate and severe	300	7.9
Pre-eclamptic toxaemia with antepartum haemorrhage	4	0.1
Eclampsia	33	0.9
Hyperemesis	17	0.4
Antepartum haemorrhage	31	0.8
Pyelitis	41	0.4
Hydramnios	22	0.6
Total	680	17.2

4.5 per cent are premature, and 19.8 per cent are $6\frac{1}{2}$ pounds or less. In cases with complications these rates are much higher, the prematurity-rate, for example, ranging from 14.9 per cent for pre-eclamptic toxaemia to 34.3 per cent for antepartum haemorrhage and 37.8 per cent for hydramnios.

Table XIII also shows, for each specific complication, the excess in the prematurity-rate as compared with the control group without complications, the standard deviation of this excess (calculated as described in Appendix A) and t, the ratio of the difference to its standard deviation. According

TABLE XIII.

All Primiparae Except Multiple Births: Cumulative percentages by Birth-weight in Cases With and Without Complications of Pregnancy.

Birth-weight		Without complications	Pre-eclamptic toxaemia	Eclampsia	All toxaemias	Pre-eclamptic toxaemia plus antepartum haemorrhage	Antepartum haemorrhage	Hydramnios
Pounds	Ounces							
Below 2	9	0.3	0.8	2.0	0.8	0.0	5.3	10.8
3	9	0.7	3.2	5.9	3.2	9.5	10.7	24.3
4	9	1.5	7.0	11.8	7.3	23.8	27.7	35.1
5	9	4.5	14.9	19.6	15.6	42.9	34.3	37.8
6	9	19.8	33.1	21.6	32.0	47.6	51.4	94.5
12	1	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Number of cases		3570	631	51	709	21	76	37
Excess per cent premature			10.3	15.1	11.1	38.4	29.8	33.3
Standard deviation of difference			2.18	9.08	2.13	22.22	10.15	12.56
t			4.83	1.66	5.26	1.73	2.93	2.66

TABLE XIV.

All Multiparae Except Multiple Births: Cumulative Percentages by Birth-weight in Cases With and Without Complications of Pregnancy.

Birth-weight		Without complications	Pre-eclamptic toxaemia	Eclampsia	All toxaemias	Pre-eclamptic toxaemia plus antepartum haemorrhage	Antepartum haemorrhage	Hydramnios
Pounds	Ounces							
Below 2	9	0.9	1.6	0.0	1.5	4.8	6.3	4.2
3	9	1.6	4.3	5.9	5.9	4.8	16.6	33.4
4	9	3.1	10.2	29.4	10.9	23.8	33.8	41.7
5	9	6.2	18.4	35.3	19.4	38.1	44.2	45.9
6	9	19.2	36.2	94.1	38.8	95.3	56.2	91.7
12	1	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Number of cases		1407	439	17	459	21	174	24
Excess per cent premature			12.2	29.1	13.2	31.9	38.0	39.7
Standard deviation of difference			3.08	23.28	3.11	20.30	7.84	20.79
t			3.98	1.25	4.24	1.57	4.86	1.91

to the usual statistical convention, where t is 2 or more the difference may be regarded as significant. This is found to be true in all complications except eclampsia and pre-eclamptic toxaemia plus antepartum haemorrhage, in which two categories the number of cases was very small. However, even in these groups, t is greater than .1.65, so the odds are at least 20 to 1 against a difference as great as that observed occurring by chance in the expected direction. The reality of the effect is further emphasized by the significant result obtained with the less severe forms of toxaemia, where many more cases are available. It may, therefore, be concluded that all these types of complication of pregnancy have a significant and marked effect in decreasing the birth-weight of infants born to primiparae. Table XIV shows that the same conclusions apply to multiparae.

The next question that arises is whether any or all of these complications exercise an adverse effect on the foetus apart from that on its birth-weight. This can be best answered by applying the method of "expected survivors," already applied in Tables X and XI to the total complication group. Table XV shows the results for cases of toxaemia, antepartum haemorrhage and hydramnios in primiparae and multiparae. In each case the standard deviation is shown (calculated as described in Appendix A) and t, the ratio of the difference between observed and "expected" survivors and the standard deviation of the difference.

For the group of all toxaemias, the differences are not all of the same sign. Premature infants, both in primiparae and multiparae, appear to do very slightly better than the controls, whereas the mature babies do worse. But none of the differences are significant, the values of t being 0.30, 0.33, 1.31, and 1.74. The differences between observed and expected survivors, taken as a whole, are no greater than would be expected from chance sampling variation. While toxaemias of pregnancy, as already shown, have a marked and significant effect in lowering the birth-weight of the infant, there is no reason to suppose that they have any other consequence that can be measured by means of survival rates.

In antepartum haemorrhage the 4 differences are all in the same direction. In every case the babies in the group with complications do worse than the controls. The differences among the premature babies are both significant, even when considered in isolation, having t values of 2.61 and 2.11. The difference for mature infants do not reach the level of statistical significance when taken individually; but the fact that they are all in the same direction strengthens the case for regarding the whole evidence as affording a very good reason indeed for concluding that the babies born of mothers with antepartum haemorrhage have a greater risk of death than their weight alone would indicate. In the third paper in this series it will be shown that death or stillbirth due to asphyxia is a common finding in cases of antepartum haemorrhage. In hydramnios, as in antepartum haemorrhage, all 4 differences are in the same direction, showing that hydramnios in the mother lessens the chance of survival in the foetus. The 2 differences for premature infants are highly significant, with t values of 7.77 and 4.01 while the differences for mature infants have t values of 1.14 and 0.80. The probability of all 4 differences in the same direction occurring by chance is very small indeed. It can be concluded that hydramnios in the mother, like antepartum haemorrhage, not only tends to induce premature labour, but also has other harmful effects on the foetus. These are more marked in hydramnios than in antepartum haemorrhage. Indeed,

TABLE XV.

Observed and "Expected" Survivors in Specified Complications.

Complications	Premature					Mature				
	Observed survivors	Expected survivors	Difference	Standard deviation difference	t	Observed survivors	Expected survivors	Difference	Standard deviation difference	t
Toxaemias:										
Primiparae	75	73.26	+1.74	5.81	0.30	570	581.47	−11.47	6.58	1.74
Multiparae	58	50.22	+7.78	5.92	1.31	350	352.07	−2.07	6.27	0.33
A.P. II.										
Primiparae	8	14.60	−6.60	2.52	2.61	40	48.53	−8.53	9.27	0.92
Multiparae	24	35.86	−11.86	5.62	2.11	80	92.37	−12.37	9.50	1.30
Hydramnios:										
Primiparae	0	4.76	−4.76	0.61	7.77	20	21.89	−1.89	1.66	1.14
Multiparae	0	4.13	−4.13	1.03	4.01	20	22.02	−2.02	2.53	0.80

TABLE XVII.

All Single Births: Cumulative Percentages by Birth-weight in Cases with Chronic Maternal Disease.

Birth-weight		No complications	All chronic disease	Cardiac disease	Pulmonary tuberculosis	Chronic chest disease	Acquired syphilis	Diabetes	Anaemia	Local disease of uterus
Pounds	Ounces									
Below 2	9	0.4	1.1	0.6	0.0	1.8	0.0	0.0	3.2	0.0
3	9	1.0	2.7	1.7	0.0	5.5	1.8	0.0	3.2	0.0
4	9	1.9	5.9	3.4	6.1	5.5	6.1	33.3	6.3	11.8
5	9	4.9	10.2	6.3	9.1	9.1	9.6	50.0	11.3	29.4
6	9	19.6	34.9	41.7	9.1	27.3	20.2	50.0	14.5	94.1
12	1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
No. of cases		4977	557	175	33	55	114	6	62	17
Excess per cent premature			5.3	1.4	4.2	4.2	4.7	45.1	6.4	24.5
Standard deviation of difference			1.93	2.32	7.30	5.50	3.85	20.40	5.59	20.30
t			3.12	0.47	0.57	0.76	1.22	2.21	1.14	1.21

no premature infants in the hydramnios group survived. The high wastage rate associated with hydramnios is largely due to the frequent occurrence of congenital defects, especially anencephalus.

B. *Acute Infection and Injuries.*

Acute infections and injuries were recorded if they occurred within 3 months of delivery. Only those conditions serious enough to be treated in hospital were included, because of the likelihood that milder conditions might not have been mentioned in many of the case notes, especially where the pregnancy and delivery were straightforward. The 71 cases included influenza, pneumonia, subacute bacterial endocarditis, acute gonorrhoea, thrombophlebitis, ischiorectal abscess, acute appendicitis, intussusception, fractures, and severe falls without fracture. Table XVI shows the percentage of premature infants born to mothers with the

TABLE XVI.

Infants Whose Mothers had Acute Infections and Injuries.

	Pre-mature Per cent	Per cent survivors Pre-mature	Mature
Mothers with acute infections and injuries	11.3	62.5	95.2
Mothers without complications	4.9	63.8	96.8

above conditions, as well as the survival rates for premature and mature babies. As might be expected, the prematurity rate is higher than in the control group. There is no evidence of any adverse effect on the infant apart from that on its birth-weight. The numbers of cases in the various diagnostic categories are too small to allow of the sub-division of the group into its individual infections and injuries.

C. *Chronic Maternal Diseases.*

Among all the primiparae and multiparae, excluding cases of multiple birth, there were 557 records of chronic conditions in the mother coincident with pregnancy, distributed as follows : —

Cardiac disease	175
Pulmonary tuberculosis	33
Chronic chest diseases (except tuberculosis)	55
Diabetes	6
Syphilis (acquired)	114
Syphilis (congenital)	32
Anaemia	62
Local disease of uterus or ovaries	17
Others	63

The term anaemia covers cases of hypochromic anaemia with a haemoglobin percentage of 50 or less, and cases of pernicious anaemia, the former being by far the more frequent. Table XVII gives cumulative percentages by weight of infants born to mothers with these diseases. The prematurity-rate for all chronic diseases is 10.2 per cent compared with the control figure of 4.9 per cent and the difference, 5.3 per cent with a t value of 3.12, is statistically significant. In each of the chronic conditions listed the prematurity-rate is increased, though not very strikingly except in diabetes and local uterine disease. In no individual group is the difference statistically significant by itself, the value of t never rising above 1.22 except in diabetes, where a t value of 2.21, based on only 6 cases, does not correspond to the conventional odds of at least 1 in 20. Nevertheless, taken all together, there is strong evidence that chronic complications have an adverse effect on the birth-weight of the infant. But the effect is not so well established, nor anything like so important quantitatively, as that observed with complications of the pregnancy itself, such as toxaemia and antepartum haemorrhage. The method of " expected survivors " was applied to the 2 largest groups, cardiac disease and acquired syphilis, to test

whether there was any adverse effect on the foetus part from that on weight. No significant difference was found between the observed and the expected numbers of survivors.

Comparison with Results of Other Workers.

All authorities are agreed as to the importance of pathological conditions in the mother acting on the infant, but opinions differ widely as to the relative prominence of the various specific complications. In most cases the results are based upon analysis of records of premature infants, or of stillbirths or deaths, without any control groups, nor is there usually any differentiation by booked and emergency admissions, primiparity and multiparity, or any clear indication of the composition of the hospital sample in relation to the general population.

Anderson, Brown and Lyon (1941) in a controlled survey of a year's births in Cincinnati General Hospital, give toxaemia, uterine bleeding and syphilis as the most important complications leading to prematurity. Diddle and Plass (1942) also specify toxaemias and syphilis as being of major importance. Tyson (1934) attributed 18 per cent of 469 premature births to syphilis, this being responsible for more premature births than any other single complication.

Most of the American authors are agreed on the importance of syphilis in the aetiology of prematurity, stillbirths and infant deaths. This is not found in the present series of cases. The prematurity-rate in syphilis, though higher than where no complications occurred, is not markedly so; and the number of cases are relatively few. In a later paper it will be shown that congenital syphilis is a comparatively unimportant cause of stillbirth and neonatal death. These results pay tribute to the good effect of the antenatal treatment which

nearly all the cases received. The importance attributed to syphilis by American investigators may be partly due to the frequency of the condition among negro mothers, who have, in any case, a higher prematurity-rate than the white population. Dunham (1939), in New Haven, U.S.A., found that the average birth-weight of white infants, as compared with negroes, was 175 g. higher in males and 337 g. in females.

The effect of maternal complications on the foetus, other than on the birth-weight, has been investigated by Breese (1938). He calculated observed and expected wastage-rates for a number of complications, which he expressed as percentages by a method essentially similar to that used in this paper. His findings were as follows:

	Observed mortality per cent	Expected mortality per cent
Pre-eclamptic toxaemia ...	27	26
Threatened abortion ...	75	67
Bleeding	65	63
Placenta praevia	46	35
Hydramnios	100	60
Syphilis	24	17
Cardiac disease	40	43

The difference between observed and expected mortality was significant only in the case of hydramnios.

FACTORS AFFECTING BIRTH-WEIGHT.

2. AGE OF MOTHER.

Table XVIII shows the percentage of infants at or below certain weight levels born to primiparous mothers in different age groups. The prematurity-rate is seen to rise with increasing age of mothers, especially after the age of 30 years. This table refers to all firstborn infants, excluding multiple births, as the incidence of twins and triplets is known to go up with maternal age.

TABLE XVIII.

All Primiparae Except Multiple Births: Cumulative Birth-weight Percentages by Age of Mother.

Birth-weight			Age of mother in years					
	Pounds	Ounces	15–19	20–24	25–29	30–34	35–39	40–44
Below	2	9	0.0	0.5	0.6	0.4	1.4	0.0
	3	9	1.1	1.2	1.4	2.5	2.9	7.4
	4	9	2.2	2.4	2.9	6.8	7.2	7.4
	5	9	5.3	5.9	5.9	13.2	15.9	18.5
	6	9	22.9	20.2	25.5	32.6	37.0	22.2
	7	9	72.1	57.2	56.5	67.1	63.0	100.0
	8	9	91.6	89.1	84.1	90.3	85.1	
	10	1	100.0	99.9	99.2	99.6	99.5	
	12	1		100.0	100.0	100.0	100.0	
Number of cases			358	2259	1359	484	208	27

Maternal age and Incidence of Complications.

In previous sections the prematurity-rate has been shown to be positively associated with complications in the mother. The relation between complication-rates and age of mother was therefore investigated. Table XIX shows percentage complication-incidence by age of mother in all primiparae, excluding multiple births. The complication-rate is seen to rise with maternal age, this being largely due to increase in the incidence of toxaemias. Chronic medical diseases, as might be expected, are also more frequent in the older mothers. The slight fall in complications after the age of 35 is based upon small numbers, and is not significant. The figures for booked primiparae only gave a smaller proportion of complications in all age groups, as would be expected, but showed similar trends for toxaemias and chronic disease.

Maternal Age and Toxaemias.

Two questions now arise :—

1. Is the rise in prematurity-rate with age due partly or entirely to the increasing incidence of toxaemias?

2. Given a mother with toxaemia, has age any effect on her chance of producing a premature baby?

Table XX sets out prematurity-rates by age of mother, sub-divided into those with with toxaemia (Column A), those without

TABLE XIX.

All Primiparae Except Multiple Births: Percentage Complications by Age of Mother.

	Age of mother in years				
	15–19	20–24	25–29	30–34	35 and over
No complications	89.1	80.2	69.7	64.9	78.3
All complications	10.9	19.8	30.3	35.1	21.7
All toxaemias	4.2	12.9	20.5	21.6	16.2
Antepartum haemorrhage ...	3.1	1.0	0.5	3.5	2.1
Hydramnios	0.6	0.4	0.9	0.2	0.9
Chronic medical diseases ...	2.8	4.4	8.4	7.3	2.6
Others	0.3	1.1	0.1	2.4	0.0
Total cases 358		2259	1358	482	235

toxaemia (Column B), and the total group (Column C). The prematurity-rate is seen to rise with age after 30 years in both the toxaemic and the non-toxaemic mothers. The effect of age of mother on the prematurity-rate cannot therefore be solely attributed to toxaemias. Column D shows that the ratio of the prematurity-rates for toxaemic and non-toxaemic mothers, at any given age-level, is approximately constant at about 2½. The figure of 4.3 for the 15 to 19 age-group is based on only 3 premature infants, and so does not differ significantly from the value at the other ages.

the Annual Reviews of the Registrar-General for England and Wales. The still-birth-rates for primiparae rose steadily with age of mother, from 27 per 1,000 in the 15 to 19 age-group to 113 in those between 40 and 45 years. Neonatal death-rates are high in very young and very old mothers. This also is in accord with general experience, for example in the survey conducted by Woodbury (1925).

<center>FACTORS AFFECTING BIRTH-WEIGHT.</center>
<center>3. LEGITIMACY.</center>

Among the primiparae studied, 495 were unmarried. The number of unmarried

<center>TABLE XX.</center>

All Primiparae Except Multiple Births: Prematurity Rate by Age in Mothers With and Without Toxaemia.

Age of mother				Column A	Column B	Column C	Column D
				Per cent premature mothers with toxaemia	Per cent premature mothers without toxaemia	Per cent premature all mothers	Ratio A/B
15 to 19	...	...	... ...	20.0	4.7	5.3	4.3
20 to 24	...	...	... ...	12.0	5.0	5.9	2.4
25 to 29	...	...	... ...	11.9	4.4	5.9	2.7
30 to 34	...	...	... ...	24.0	9.8	13.2	2.5
35 and over	...	...	...	31.6	13.2	16.2	2.4

<center>TABLE XXI.</center>

All Primiparae Except Multiple Births: Outcome by Maternal Age.

Age of mother	Premature			Full time		
	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
Under 20	60.9	26.1	13.0	97.4	1.5	1.1
20 to 34	66.4	14.7	18.9	97.1	0.8	2.1
Over 34	63.8	14.9	21.3	92.4	1.3	6.3

Outcome by Age of Mother.

Table XXI shows the outcome for premature and mature infants by age of mother. Stillbirth-rates rise steadily with age. This is in agreement with the experience for the country as a whole, as shown, for example, in the figures calculated by Woolf (1946) from the data for 1939–40 in

multiparae was too small to allow of any valid comparison to be made with the corresponding married group, especially as the majority of unmarried mothers gained admission on this ground alone, whereas the married women usually had some complication. The present section therefore deals with primiparae only.

The distributions of weight of legitimate and illegitimate first births, excluding multiple births, are shown in Table XXII. Among the illegitimate 8.1 per cent were premature, compared with 6.9 per cent among the legitimate babies. It has already been shown that complication-rates and maternal age have an important bearing on the weight of the infant. Both these factors must therefore be examined.

under the age and over the age of 25 years. For the younger women, the prematurity-rate is the same in 2 groups; but at ages 25 and over, unmarried mothers have an excess of 5.9 per cent over the married. The difference is not statistically significant, but the t value of 1.29 indicates that a deviation as great as this would not happen by chance more than once in 10 trials. This high prematurity-rate in the older un-

TABLE XXII.

Birth-weight Percentages in Unmarried and Married Primiparae Excluding Multiple Births.

Birth-weight				Unmarried mothers		Married mothers	
Pounds	Ounces	Pounds	Ounces	Per cent	Cumulative per cent	Per cent	Cumulative per cent
	Below 3		9	1.2	1.2	1.5	1.5
3	9 to 5		8	6.9	8.1	5.4	6.9
	Over 5		8	91.9	100.0	93.1	100.0

Complication-Rates.

Unmarried mothers were found to have a total complication-rate of 19.4 per cent, being 5 per cent lower than that of the married group. This is entirely due to the low toxaemia rate of 8.7, which is just over half that of the married women (15.9 per cent). This is probably due to the younger age-composition of the unmarried mothers, and to the higher proportion in the un-booked cases admitted for social reasons rather than complications. The incidence of antepartum haemorrhage is over twice as high in the unmarried group, being 3.2 per cent as compared with the married rate of 1.4 per cent. This is possibly due to a higher incidence of mechanical interference in this group.

Age of Mother.

The average age of the unmarried mothers was 26.2 years, compared with 28.1 years for the married. Table XXIII shows the percentage of premature babies born to married and to unmarried mothers

married mothers may be associated with the fact that they have often a considerably harder time than the younger girls. The young girl is more often accepted back into the family circle, and preference is all given to younger girls for admission to homes for the unmarried.

TABLE XXIII.

Percentage Premature Married and Unmarried Primiparae Excluding Multiple Births.

	Mothers under 25	Mothers 25 and over
	Per cent	Per cent
Married mothers	5.8	8.3
Unmarried mothers	5.8	14.2
Difference		5.9
Standard deviation		4.57
t		1.29

Prematurity-rate.   Allowing for Age and Complications.

From their lower complication-rate and younger age-composition, one would expect the unmarried mothers to have a lesser incidence of prematurity than the mar-

ried, rather than the greater rate actually observed. Table XXIV shows the calculation of the number of premature babies that would be expected in the unmarried group, if at each age and complition-level they had the same chance of

6.5919 per cent. Similarly, considering complications alone, the lower incidence among the unmarried would lead to a prematurity-rate of 6.7779 per cent. When both these favourable influences are taken into account, the expected prematurity-

TABLE XXIV.

All Primiparae Except Multiple Births: Comparison of Premature Rates in Married and Unmarried Mothers, Allowing for Age and Complications.

(a) *Allowance For Age Differences*

Age of mother	Married mothers, per cent premature	Unmarried mothers, total	Number of prematures expected
15 to 19	5.38	98	5.27
20 to 24	5.84	263	15.36
25 to 29	5.79	78	4.52
30 to 34	12.91	30	3.87
35 to 39	13.97	25	3.49
40 to 44	12.12	1	0.12
Totals		495	32.63
Percentage of prematures expected		6.5919	

(b) *Allowance for Differences in Incidence of Complications*

Complication	Married mothers, per cent premature	Unmarried mothers, total	Number of prematures expected
Toxaemias	14.86	43	6.39
Antepartum haemorrhage	35.00	16	5.60
Others	11.04	37	4.08
None	4.38	399	17.48
Totals		495	33.55
Percentage of prematures expected		6.7779	

(c) *Method of Calculation.*

Percentage of prematures in married group ... ... $= 6.9573$

Expected percentage of prematures in unmarried group after allowing for age and complication differences $= \dfrac{6.5919 \times 6.7779}{6.9573}$

$= 6.4219$

Expected number of prematures ... ... $= 6.4219$ per cent of 495

$= 31.8$

Observed number of prematures ... ... $= 40.0$

Excess ... ... $= 8.2$

bearing premature infants as obtains in the married mothers. The actual prematurity-rate among the married women was 6.9573 per cent. If allowance is made for age only, the more favourable age composition of the unmarried women would lead one to expect a lower prematurity-rate, namely

rate is 6.4219 per cent, giving an expected number of premature infants of 31.8, against the 40 actually observed. The excess of 8.2 prematures among the unmarried mothers must be due to causes other than age or complications.

The difference is not statistically signifi-

cant, being only just above its standard deviation. It is nevertheless suggestive, when considered in connexion with the observations of other workers such as Toverud (1933), who, discussed the effect of illegitimacy on the weight and maturity of the infant, using as his material cases admitted to a home for unmarried mothers in Oslo. Over a period of 2 years the inmates received systematic prenatal care and an optimum diet. It was found that mothers admitted 2 months or more before delivery had larger babies than those admitted for 6 weeks or less, and those again had heavier infants than mothers admitted just before delivery. The average birth-weights in the 3 groups were 3,587 g., 3,347 g., and 3,240 g., giving a difference between the first and third groups of about three-quarters of a pound.
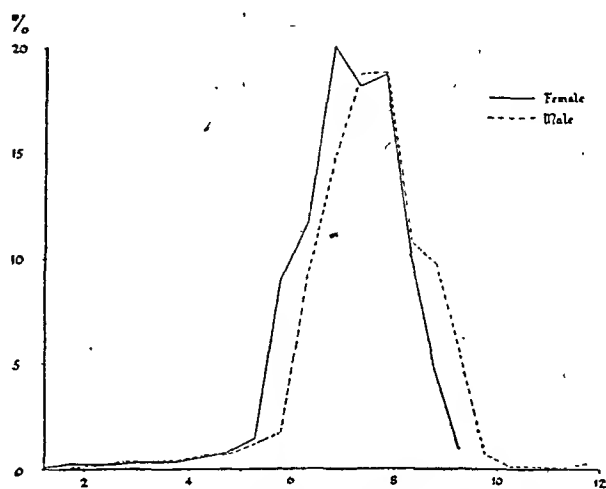

FIG. 6.
Distribution of birth-weight by sex.

FIG. 7.
Survival-rates according to sex of infant.
Outlined rectangles—Females.
Black rectangles—Males.

FACTORS AFFECTING BIRTH-WEIGHT.
4. SEX.

Fig. 6 shows the percentage distribution of male and female primiparous births according to weight. If one takes the usual limit of prematurity—5 pounds 8 ounces or less—6.7 per cent of the firstborn male babies would be classed as premature, and 7.5 per cent of the females, a difference of 0.8 per cent. Among the multiparae, the figures are 10.7 per cent for the males and 13 per cent for the females with a difference of 2.3 per cent. At weights of $6\frac{1}{2}$ pounds or less, the excess for females among firstborn is 10.3 per cent, and 14.2 per cent for multiparae. It would probably be more accurate to adopt a different weight standard of prematurity for male and female infants, since female infants of the same gestation time would certainly tend on the average to be lighter than male babies. This is, however, a matter for general agreement. In this paper, the standard criterion will be adhered to.
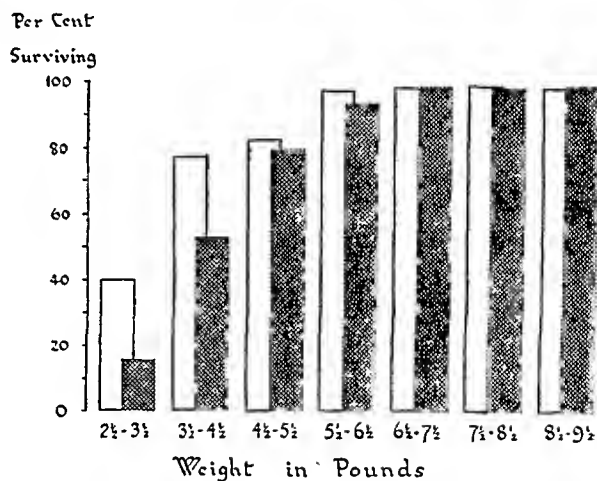
Outcome of Sex and Weight.

Tables XXV and XXVI give comparative figures of outcome by birth-weight in male and female infants. The data for survival-rates given in Table XXV, which relate to primiparae, excluding multiple births, are shown in Fig 7. Girl babies have a much higher survival-rate among the premature and smaller mature-weight groups. This is due to the decreased wastage from deaths. The death-rate for

male firstborn premature infants was 23.8 as compared with 6.1 per cent for female. Among multiparae the rates were 25 per cent for males and 14.8 per cent for females. The stillbirth-rate was slightly

rate among all primiparae was 8.6 per cent, and 5.9 per cent when emergency cases, illegitimate births and multiple births were excluded.

Outcome and birth-weight. Outcome—

TABLE XXV.

Primiparae Except Multiple Births: Outcome by Weight and Sex.

Birth-weight				Male infants			Female infants		
Pounds	Ounces	Pounds	Ounces	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
	Below	2	9	0.0	62.5	37.5	0.0	20.0	80.0
2	9 to	3	8	15.4	50.0	34.6	40.0	5.0	55.0
3	9 to	4	8	52.5	27.5	20.0	77.1	0.0	22.9
4	9 to	5	8	79.1	10.5	10.5	81.7	6.5	11.8
5	9 to	6	8	92.2	3.8	4.0	96.2	1.1	2.7
6	9 to	7	8	97.3	0.5	2.2	97.2	1.0	1.8
7	9 to	8	8	97.1	0.4	2.5	97.7	0.7	1.6
8	9 to	10	0	97.3	1.0	1.7	97.2	0.0	2.8
10	1	and over		66.7	0.0	33.3			

TABLE XXVI.

Multiparae Except Multiple Births: Outcome by Weight and Sex.

Birth-weight				Male infants			Female infants		
Pounds	Ounces	Pounds	Ounces	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
	Below	2	9	0.0	46.2	53.8	0.0	26.3	73.7
2	9 to	3	8	10.5	42.1	47.4	26.7	26.7	46.6
3	9 to	4	8	45.3	24.5	30.2	68.6	14.3	17.1
4	9 to	5	8	70.2	12.8	17.0	81.0	5.2	13.8
5	9 to	6	8	76.9	8.7	14.4	93.7	0.5	5.8
6	9 to	7	8	94.4	1.2	4.4	97.1	1.1	1.7
7	9 to	8	8	96.9	0.5	2.6	96.5	0.0	3.5
8	9 to	10	0	94.7	0.0	5.3	97.1	0.0	2.9
10	1	and over		90.9	0.0	9.1			

higher than the male in firstborn premature infants, and about the same in the multiparae.

In a later paper, male and female death-rates by pathological cause will be compared.

SUMMARY.

A statistical analysis has been made of nearly 8,000 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive.

Prematurity rates. The prematurity-

whether the infant was stillborn, died or survived—was closely related to birth-weight, wastage decreasing from 100 per cent for babies under 2 pounds 9 ounces to about 3 per cent for babies over 6 pounds, with a rise for postmature births. In the smallest babies stillbirths constituted about half the total wastage, the proportion rising to 80 per cent for mature and 100 per cent for postmature infants.

Complications of pregnancy. The prematurity-rate among mothers with complications was 3 times as high as among those

without complications. In complications of the pregnancy itself, the prematurity-rates were: toxaemias, 15.6 per cent; ante-partum haemorrhage, 34.3 per cent; hydramnios, 37.8 per cent. In mothers without complications the rate was 4.5 per cent. The most common chronic diseases coincident with pregnancy were cardiac disease, syphilis and anaemia. For mothers with chronic conditions the prematurity-rate was 10.2 per cent. Chronic medical diseases are far less important causes of prematurity than complications of pregnancy itself.

The increased mortality of babies of mothers with toxaemia and chronic medical disease is entirely accounted for by the decrease in birth-weight, but babies of mothers with antepartum haemorrhage and hydramnios have an extra risk when the effect of reduced weight is taken into account.

Age of mother. Prematurity-rates increase with age of mother. This is partly due to increased incidence of toxaemias. Stillbirth-rates also rise with maternal age but neonatal death-rates are higher in the younger and older age-groups.

Legitimacy. Illegitimate babies had a higher prematurity-rate than the legitimate, accounted for by an increase in the group of older unmarried mothers.

Sex. Girl babies on the whole are smaller than boys at birth, but have a lower death-rate. Stillbirth-rates were approximately the same in the two sexes.

It is a pleasure to thank Professor C. McNeil and Mr. W. F. T. Haultain for permission to use paediatric and obstetrical records; Mrs. W. Lord, B.A., and Miss Joyce Thomson for assistance in the analyses and computations; Dr. Barnet Woolf for advice on the planning of the investigation and on the statistical methods used; and Professor McNeil and Professor R. W. B. Ellis for their interest and encouragement.

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APPENDIX A.

STATISTICAL METHODS.

The variance of a percentage, p, based on a total sample $= n$, was calculated by the usual formula, $V_p = p(100 - p)/n$.

The variance of the difference between two percentages is the sum of the variances of the individual percentages, and the standard deviation of the difference is the square root of this figure.

In many of the percentages and the " expected numbers ", part of the births, namely those of the mature infants who survived, were sampled on a 1 in 10 basis. It is necessary to allow for this in calculating variances. Suppose the data on which the calculation rests to be as follows:

	Full sample	1 in 10 sample
" Successes "	a	b
" Failures "	c	d

Let the percentage of of successes be p, so that $p = 100(a + 10b)/(a + 10b + c + 10d)$. Then the variance of the observed number, $(a+10b)$, is

$$\frac{(a+10b)^2 \; (c+100d) \; + \; (c+10d)^2 \; (a+100b)}{(a+10b+c+10d)^2}$$

And the variance of p is

$$\frac{p^2 \; (c+100d) \; + \; (100-p)^2 \; (a+100b)}{(a+10b+c+10d)^2}$$

The variance of the difference between the observed and the " expected " number in a composite of various independent groups, such as birth-weight groups, is the sum of the variances of the individual observed and " expected " numbers in each of the groups. The variance of the observed number, in cases where the sampling is full, is $p.q \; (p+q-1)$ where $p =$ number of " successes " and $q =$ number of " failures ".

The variance of the " expected " number is variance of the expected rate multiplied by $(p+q)^2$, the formula for the variance of the expected rate being $z(1-z)/(n-1)$, where $z =$ proportion of successes in control group and $n =$ number of cases in control group.

When the observed and expected figures are based on data of which part are sampled on a 1 in 10 basis, the formula for the variance of the observed number is

$$\frac{(a+10b)^2 \; (c+100d) \; + \; (c+10d)^2 \; (a+100b)}{A^2+B-2AC/B}$$

where a, b, c and d have the meanings specified above, and

$$A = a+c+10(b+d)$$
$$B = a+c+100(b+d)$$
$$C = a+c+1000(b+d)$$

The variance of the " expected " number is the variance of the expected rate multiplied by A^2, the variance of the expected rate being calculated from the data in the control group using the last formula given above, but made to apply to the rate by dividing the result by the square of the number in the control sample corresponding to A in the sample being standardized.

The derivation of the above formulae is in course of publication.

B. Woolf.

The Influence of Semen on the Female Reproductive Organs

BY

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Our experiments were started in 1942. They were based upon the clinical experience of one of us (G.-A.) who had observed that the uterus and upper third of vagina of many young virginal women at the time of marriage was abnormally small. Such uteri grew however to their accredited normal size within a few months of married life provided no contraceptives were used which interfered with the absorption of semen from the vagina. *Per sequitur* if sheath or withdrawal methods of contraception were employed such uterine development did not take place. Following the dictum of William Harvey to seek and search out the secrets of nature by way of experiment, the purpose of our research was to discover any scientific explanation for this observation, that is, does absorption of semen produce any effect upon the genitalia.

Preliminary experiments were carried out using semen kindly supplied by Dr. Scott Wilson of the Harley Street Laboratories. At that time no special attention was paid to the nature of the specimens proffered. Some were several days old and therefore infected or biochemically altered. Others were defective as regards the number and quality of spermatozoa present. Despite this, results were encouraging. It is necessary to refer briefly to these experiments (Green-Armytage, 1943) because they represent the basis on which further investigations have rested and have guided the plan of the later research.

It is generally agreed that if female litter mates have been and are being kept under identical conditions their reproductive organs are equally developed and are of the same length and width. Therefore in order to obtain a reliable measure for assessing the results of treatment, we have used only does of the same litter in any of these experiments, keeping one of each litter as a control and comparing our findings in the animals subjected to treatment with those of their respective untreated sisters.

Experiment 1. A 10-weeks-old rabbit doe was injected with 1 ml. of human semen on 3 consecutive days. Twenty-four hours after the last injection this animal and its control litter mate were killed by air embolism. The ovaries of the injected rabbit were large and showed some distinct *Blutpunkte* and on histological section there were numerous large follicles, some of which were haemorrhagic. Its uterus, as compared with that of the control, had increased in length and width, its lumen was filled with mucus; on microscopical examination the uterine muscular coat appeared to have thickened and its mucosa was oedematous.

Experiment 2 was a repetition of No. 1, but yielded a negative result.

Experiments 3 and 4. Two litters (a and b), one comprising 2, the other 3, female rabbits were spayed when 14 weeks old. Three weeks later, keeping one doe of each litter as a control, the rest were given 8 injections of 1 ml. human semen intravenously within the next 19 days. On the 20th day all the animals were killed. The uteri of the injected doe of litter (a) and of 1 doe of litter (b) were dark red and markedly larger than those of their respective controls. Their lumina were

filled with a mucoid mass and sections revealed increased width of the muscular coat with oedema and hyperaemia of the mucosa. The third rabbit of litter (b), although injected in the same way as its litter mate, showed a poor response, its uterus being somewhat longer but hardly thicker than that of the control. There was also no histological evidence of any effect on the uterine muscle or mucosa.

Experiment 5. A litter of 3 female rats, 6 weeks old, was used. Two animals received daily intra-peritoneal injections, one of 0.2 ml., the other of 0.4 ml. of human semen. On the third morning the first was found dead, whereas the vagina of the other had opened and a smear of its mucoid contents revealed the presence of epithelial cells. Twenty-four hours later leucocytes were prevailing. On the 5th day (105 hours after the first injection) the experiment was terminated. The ovaries and the uterus of the rat which had been injected were larger than the respective organs of the control. The uterus and vagina were filled with mucus. Histology of the ovaries showed the presence of numerous ripe and maturing follicles.

Experiments 6, 7, and 8 were carried out with litters of immature rats which were spayed 5, 7 and 14 days respectively before the first injection.

Experiment 7 yielded a negative result.

In experiment 6, vaginal opening occurred in one rat after the 5th, in the second after the 7th, injection but no oestrous response was observed in any of the vaginal smears which revealed only the presence of large epithelial cells in a mucoid stringy mass. Twenty-four hours after the 10th injection of 0.4 ml. of human semen both rats together with their untreated litter mate were killed. The uteri of the injected animals had markedly increased in length and width in comparison with the uterus of the control.

In experiment 8, vaginal opening was observed in all 3 injected rats after the 6th injection. Only dioestrous response was obtained. At autopsy uteri and vaginae were filled with sticky mucus. The uteri were plum coloured, long and wide. Histological comparison of the uteri of the injected and untreated animals showed increased width of the muscular coat and an increased number of glandular tubules in the hyperaemic and oedematous mucosa.

From 5 similar experiments carried out on mice, 3 yielded positive and 2 negative results.

SUMMARY.

In 9 out of 13 experiments the injection of heterologous semen had caused a marked effect on the female genitalia. From this we drew the conclusion that semen probably contains an active principle apart from its fertilizing potency which under favourable circumstances has a stimulating effect upon the female genitalia. To these preliminary investigations one of us referred in his paper (Green-Armytage, 1943), stressing the fact that further experiments were necessary to elucidate the process or processes involved. The aim of these experiments was to gather facts with a view to

(a) Defining as clearly as possible the stimulating action of semen on the ovaries and uteri, and the conditions in which such an effect can be obtained.

(b) Establishing whether, and if so to what extent, the effect upon the uterus is dependent upon the ovaries.

(c) Determining the causes of the discrepancies observed in our preliminary experiments, that is to find out why in a comparatively high percentage of the experiments the female genitalia were not influenced by the injections.

(d) Investigating whether, and if so how, hypophysectomized animals react to semen injections.

The difficulties of obtaining the necessary animals together with war-time and post-war conditions caused a regrettable delay. In this paper we are giving a report upon experiments concerned with the problems summarized under (a) and (b).

I. Human semen injected into immature animals.

This series comprises 22 experiments on immature rats and rabbits. The injected

TABLE I

No.	Species and Size of Litter	Treatment	Results					
			Ovaries		Uteri			
			Macroscop. Appearance	Histolog. Findings	Macroscop. Appearance	Histological Findings	Vagina	Remarks
1	2 rabbits 1 inj. 1 control	1 ml. HS i.v. d.×6	Cy+ S+	FoM++ Lut+++	S+ Hyp++ LMuF D+	Hyp+++ gl. tub+++ Ed+ Musc.++ cub++v		
2	3 rabbits 2 inj. 1 control	1 ml. HS i.v. d.×10	Cy+ S±	FoM+R	S+ Hyp++ LMuF D+	Hyp+ gl. tub+++ Ed+ Musc.+++		
3	5 mice 3 inj. 2 controls	0.2 ml. HS×2 i.m. d.×5	S+	FoM+++ Lut+	S+ Hyp+ D++	Hyp++ Ed+ gl. tub.+++	open 3rd day dioestrus contr. clsd. throughout	
4	2 rabbits 1 inj. 1 control	1 ml. HS i.v. d.×8	S+	FoM+R	L+	gl. tub.+ Musc.+		
5	3 rabbits 2 inj. (1)(2) 1 control (3)	1 ml. HS. i.v. a.d.×6	(1) S± C+ (2) S—	(1) FoM+R (2) FoM+R	(1) L+ (2) L++	Musc.+ as control		
6	3 rabbits 2 inj. 1 control	2 ml. HS i.v. d×6	Cy+ S+	FoM+++ Lut+++	S+ Hxp++ LMuF D++	Hyp+ gl. tub.+++ Ed+ Musc.++ cub++v		
7	6 rats 4 inj. 2 controls	0.3 ml. HS i.m. d.×5	S+	FoM+++	S+ Hyp+	Hyp+ gl. tub++ Musc.++	open (1) 36 hrs. (2, 3) 48 hrs. (4) 60 hrs. Dioestrus throughout con. cld. throughout	
8	3 rabbits 2 inj. (1)(2) 1 control (3)	1 ml. HS i.v. d.×6	(1) S— Cy+ (2) S±	(1) FoM+R (2) FoM+R	L++ L+	as control as control		
9	2 rabbits 1 inj. 1 control	1 ml.— 2 ml.—HS i.v. 3 ml.— successive days	S+	FoM+++ Lut+	S+ Hyp+ LMuF D++	Hyp+ gl. tub+++ Ed+ HR		Fig. 1, 2

TABLE I (*Continued*)

No.	Species and Size of Litter	Treatment	Ovaries Macroscop. Appearance	Ovaries Histolog. Findings	Uteri Macroscop. Appearance	Uteri Histological Findings	Vagina	Remarks
10	3 rabbits 2 inj. (1) (2) 1 control (3)	1 ml. HS i.v. d.×8	(1) S−Cy+ (2) S−	FoM+R FoR	L+ L+	gl. tub+ Musc.± Musc+		
11	3 rabbits 2 inj. (1) (2) 1 control (3)	0.6 ml. HS i.v. d.×8	(1) S± Cy+ (2) S−	FoM+R FoR	L+ L++	as control Musc+		
12	3 rabbits 2 inj. 1 control	2 ml. HS i.v. a.d.×4	S+	FoM+++	S++ Hyp+ LMuF D+	Hyp++ gl. tub+++ Ed+ H col.		
13	2 rabbits 1 inj. 1 control	1 ml. HS i.v. a.d.×8	S+	FoM+++ Lut+	S++ Hyp+ LMuF D++	Hyp++ gl. tub.+++ Ed+ H col.		
14	2 rabbits 1 inj. 1 control	1 ml. HS i.v. a.d.×6	S±	as control	L+	Musc.+		

KEY TO TABLES.

inj. injected.
contr. control (not injected).
i.v. intravenously.
i.m. intramuscularly.
s.c. subcutaneously.
d. daily.
a.d. alternate days.
HS. human semen.
HoS. homologous semen.
S. size (length and width) compared with control.
S− smaller than control.
S± equal to control.
S+ (++, +++) bigger (increasing) than control.

L. length.
L± equal to control.
L+ (++, +++) longer (increasing than control.
D+ diameter increased, compared with control.
Cy+ cystic.
FoM. follicle stimulation.
FoR retardation of follicle development.
FoM+R few mature follicles present but majority of follicles less developed than controls.
- controls.

Lut. luteinization.
Hyp. hyperaemia.
LMuF. lumen dilated and filled with mucus.
Es. oedema.
H.col. high columnar epithelium.
cub. cuboidal epithelium.
v. vacuoles in epithelial cells.
gl. tub. +(++, +++) increased number of glandular tubules present.
Musc.+ thickness of muscular coat (compared with controls).

HR. haemorrhage.
RO. right ovary.
LO. left ovary.
BOE. both ovaries removed.
ROE. right ovary removed.
LOE. left ovary removed.
RH. right uterine horn.
LH. left uterine horn.
RhE. right uterine horn removed.
LHE. left uterine horn removed.
NAD. no abnormality detected.
BA. beginning atrophy.

material was human semen as collected in Sterility Clinics and Laboratories regardless of whether the specimens were produced by healthy donors or otherwise. Eight experiments were negative, that means to say in these 8 assays no difference was found between the ovaries and uteri of the injected animals and those of their litter mates kept untreated as controls.

As will be seen from Table I, in 5 experiments on rabbits, in 1 on rats and in 1 on mice, the autopsy—performed 24 hours after the last injection—revealed an increase in the size of the ovaries, and on histological examination numerous ripe as well as maturing Graäfian follicles were found. In 5 instances a more or less extensive luteinization was noticed. The uteri of the injected does had increased considerably in length and width. They appeared dark red. Their lumen was distended and blocked by congealed mucus. Microscopical examination revealed hyperaemic and oedematous mucous membranes piled up in folds with numerous glandular tubules in each visual field, a stroma rich in cells and a lining epithelium which was either columnar or consisting of two or three layers of cuboidal cells. These epithelial cells as well as those of the glandular tubules often contained vacuoles. Figs. 1 and 2 show the result of such an experiment which was of special interest because of a haemorrhage into the uterine mucosa causing a partial shedding off of the lining epithelium.

Quite different from these findings were the results in other experiments of this series. In these the ovaries of the injected does were either smaller than or of about the same size as the ovaries of the controls. Often small cysts containing a light pink-tinted fluid were observed on their surface. The uteri were usually much longer than their controls but they appeared white, narrow and thread-like. Histological examination of the ovaries showed the presence of few (mostly 2 or 3) large ripe, or almost ripe, Graäfian follicles contrasting with the rest of the follicles which appeared smaller, being at an earlier state of development than the partly-matured follicles in the controls. Microscopical slides of the uterine wall revealed usually little difference between the injected and the control litter mates. Sometimes a moderate increase in the width of the muscular coat was noted but no change in the mucosa.

II. *Human semen injected into spayed mature animals.*

This series consisted of 14 experiments but in only 5 of them striking differences between the injected does and their similarly-spayed litter mates were observed. These successful experiments have been summarized in Table II. It will be seen from this table as well as from Figs. 3, 3c, 4 and 4c, that the atrophic changes in the uterine wall which follow castration were prevented. At autopsy the uteri of the control does were found in varying stages of atrophy, whereas the uteri of the injected animals were hypertrophied and hyperaemic. Histological examination showed that the width of the muscular coat and of the mucosa had increased. The latter was oedematous; its superficial layer rich in intensely stained cells. There were numerous glandular tubules and the epithelial lining consisted of large high columnar cells.

Twice we have repeated these experiments using litters of mature as well as of immature rabbits. (1) Of 12 immature does 3 gave results similar to those recorded in Table II, 5 completely failed to respond to the injections, whereas the uterine horns of 4 injected rabbits were found to have increased in length but not in width. These were much longer than those of their respective untreated litter mates, but histo-
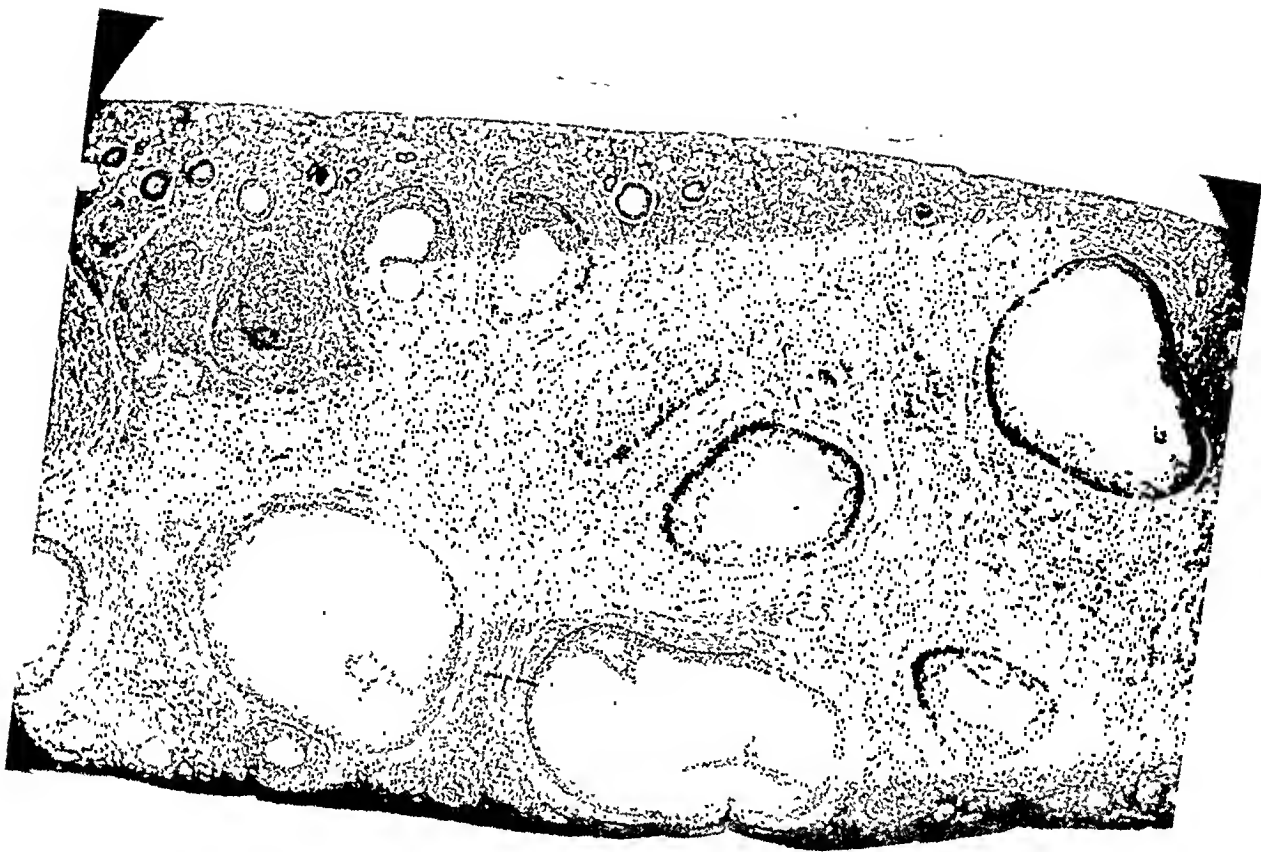
FIG. 1.

Section through an ovary of a 7-weeks-old rabbit after 3 intravenous injections of 1, 2, and 3 ml. respectively of human semen on 3 successive days. Note numerous mature and almost mature Graafian follicles and a certain degree of luteinization of theca cells.
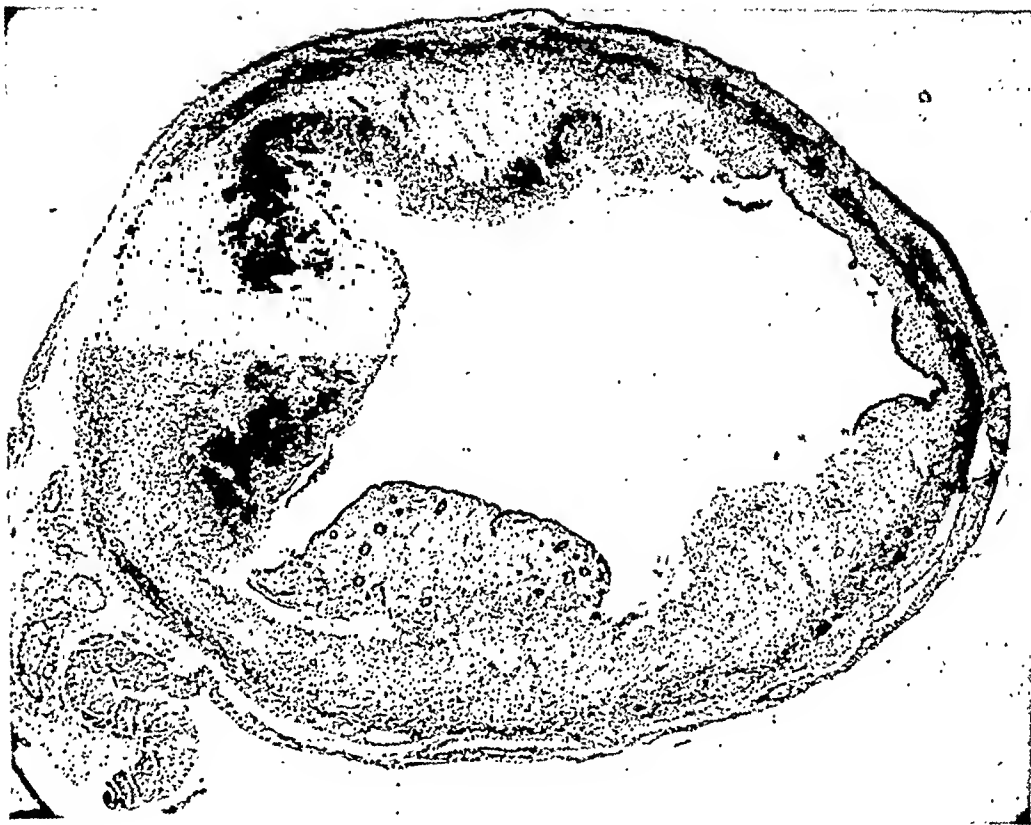
G. A.

Fig. 2.

Section through the uterine horn of the same rabbit (see Fig. 1).
Note hyperaemia and oedema of the mucosa, the increase in the number of glandular tubules and the haemorrhages into the mucosa, the epithelial layer of which is partly shed.
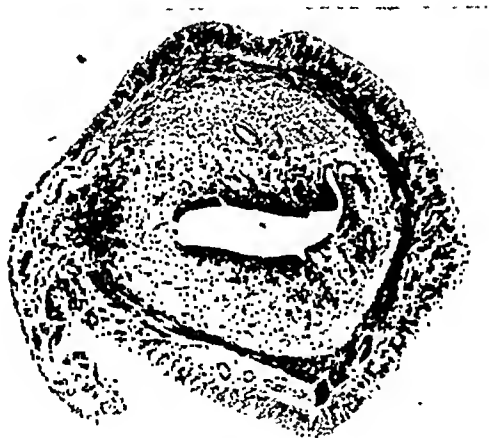
G. A.

FIG. 3 and 3C.

Sections of the uteri of 2 litter-mate does spayed 24 hours before the experiment was started. "3" received 8 intravenous injections of 1 ml. human semen on alternate days. "3c" is the untreated control.

Note difference in the thickness of muscular coats and mucous membranes between "3" and "3c".
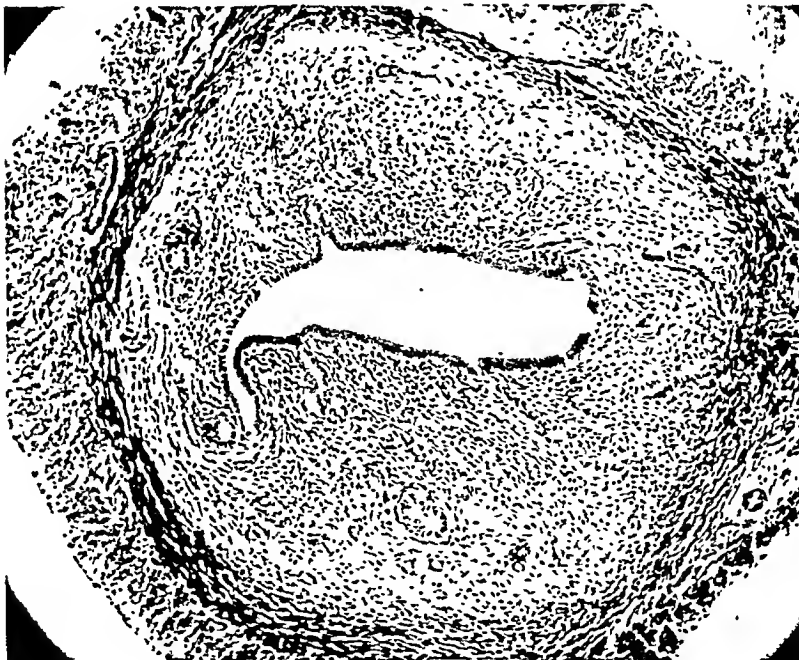
G. A.
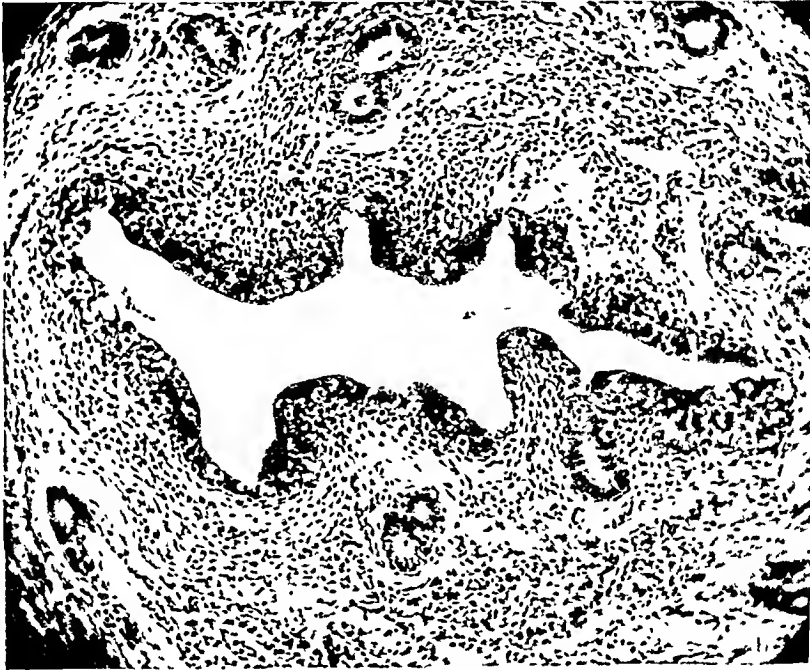
PLATE 27

FIG. 4 and 4c.

High magnification of " 3 " and " 3c ".

Note the number of glandular tubules in the oedematous mucosa in " 4 ".
The epithelial lining consists of 2 or 3 layers of large cells, many of which
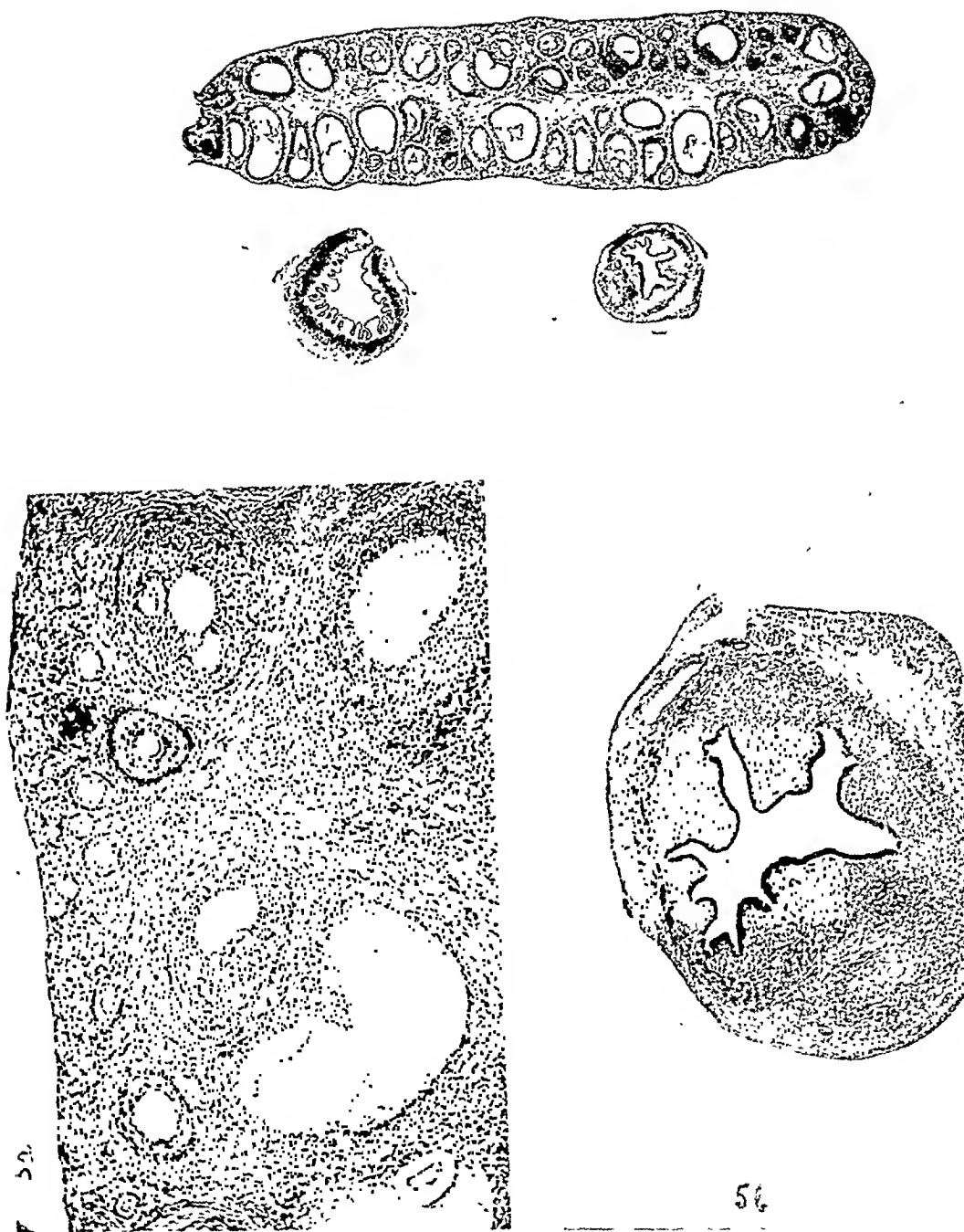contain vacuoles.

G. A.

FIG. 5, 5a, and 5b.

Sections through the ovary and uterine horn of a 7-weeks-old rabbit after 3 intravenous injections of 0.8 ml. of homologous semen given on successive days.
Note follicle stimulation and increased thickness of the uterine wall.

G. A.

FIG. 6.

Uteri of 2 litter-mate does, 3 months old, spayed 1 week before the experiment started. " C " is the uterus of the untreated control.

The uterus pictured on the left was removed 24 hours after the last of 3 intravenous injections of 1 ml. homologous semen given on alternate days. Note difference in the size of the 2 uteri.
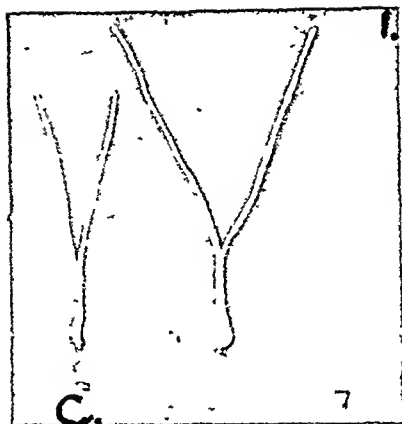
G. A.

FIG. 7.

Uteri of 2 litter-mate does, 3 months old, spayed 3 weeks prior to the experiment. "C" is the uterus of the untreated control. The experimental animal received 8 intravenous injections of 0.8 ml. of homologous semen.

Note increase in length but not in thickness.

G. A.

FIG. 8.

Section through left ovary of an 8-weeks-old rabbit removed 24 hours before the first of 7 intravenous injections of o.8 ml. of homologous semen given on alternate days.

FIG. 9.

Section through the right ovary of the same rabbit (Fig. 8) removed 24 hours after the last injection.

Note in Fig. 8 a fair number of maturing follicles in an approximately equal state of development.

Note in Fig. 9 two mature follicles but absence of further maturation in the other follicles as compared with Fig. 8.
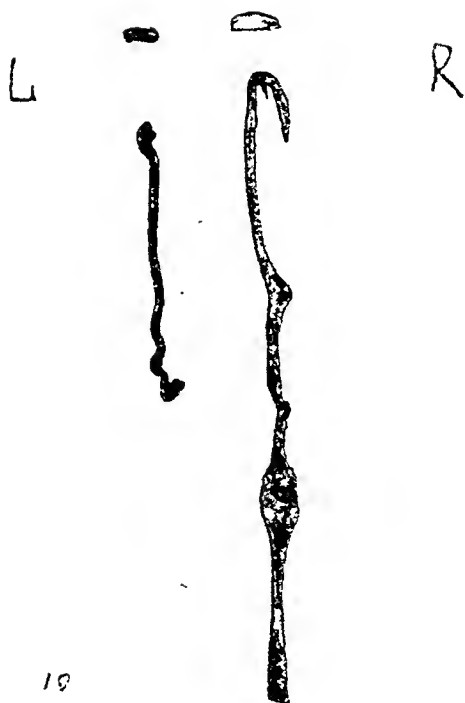
Fig. 10.

L = left ovary and uterine horn of a 2-months-old doe removed 24 hours prior to the start of the experiment.

R = right ovary and uterine horn of the same rabbit removed 36 hours after the last of 4 intravenous injections of 1.0 ml. of homologous semen given on alternate days.

Note increase in size of the right ovary and uterine horn.

G. A.

FIG. 11.

Ovaries and uteri of 3 litter-mate does, the right ovaries and uterine horns of which had been removed 24 hours prior to the start of the experiment (marked C). One doe (marked S) received 6 intravenous injections of 0.8 ml. of homologous semen given on successive days The second doe (marked CB) received 6 intravenous injections of 0 8 ml. of the same semen after it had been heated in a boiling water bath.

The third doe (marked CN) received 6 intravenous injections of 0.8 ml. of normal saline.

The left ovaries and the corpora uteri with the remaining uterine horns were removed 24 hours after the last injection.

Note: In CN right ovary slightly larger than left. In CB ovaries of equal size, but right horn is larger than left. In S left ovary is larger and left uterine horn is much longer than right but there is no increase in thickness. Increase in size of the corpora uteri and vaginae of CB and S.

G. A.
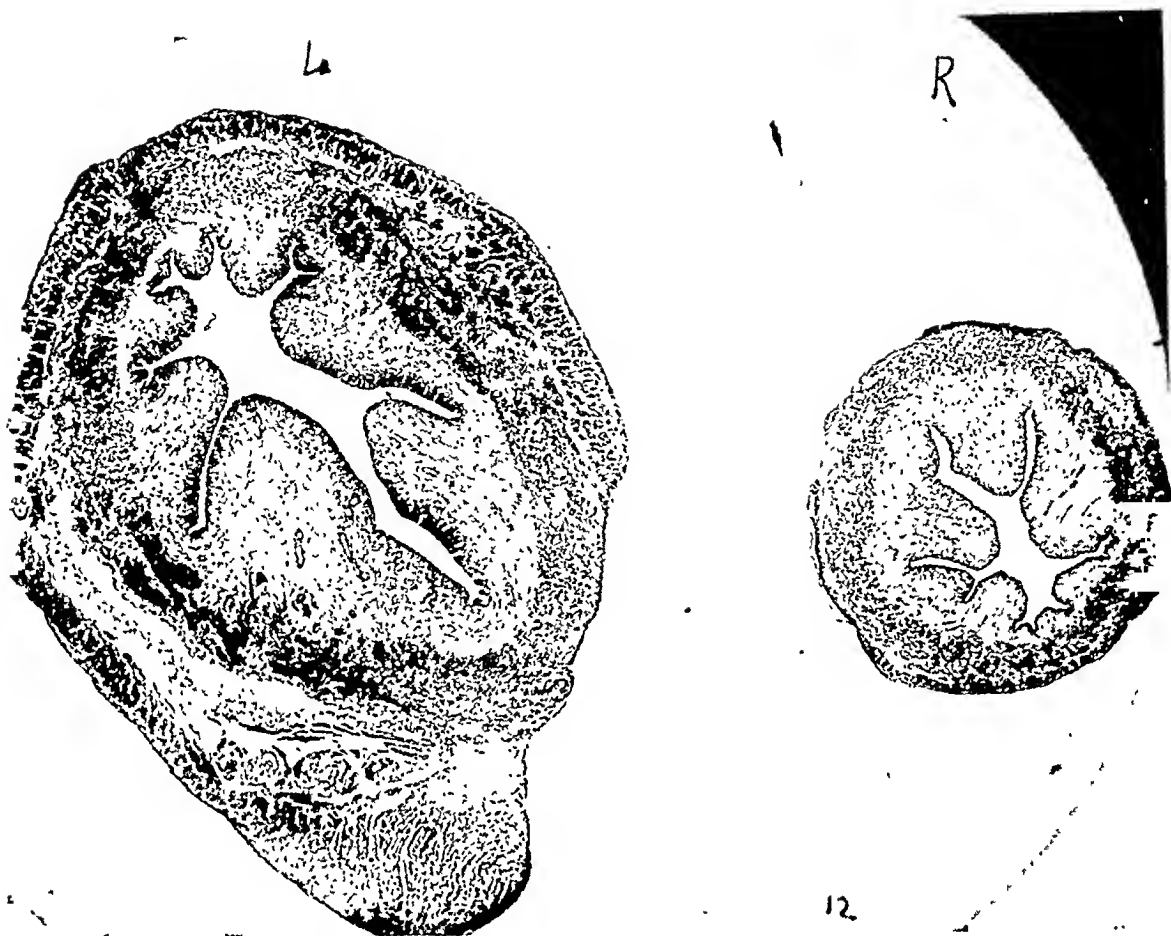
FIG. 12.

Sections through the right (R) and the left (L) uterine horn of an 8-months-old rabbit spayed 4 weeks prior to the start of the experiment.

R was removed 24 hours before the first injection. L was removed 24 hours after the last of 7 intravenous injections of 1 ml. of homologous semen given on alternate days.

Note the difference in diameters between L and R caused by a marked increase in the thickness of the muscular coat and the mucosa in L. Note also the engorged blood vessels, the increase of glandular tubules and the cellular infiltration of the mucosa in L.

G. A.

FIG. 13.

Uterine horns of a 4-months-old doe, spayed 1 week prior to the start of the experiment. The right uterine horn (R) was removed 24 hours before the first of 8 intravenous injections of 0.9 ml. of homologous semen given on successive days. The left uterine horn (L) was removed 24 hours after the last injection.

Note increase in length and width of the (L) horn.

G. A.

TABLE II.—SPAYED MATURE ANIMALS

No.	Species and Size of Litter	Treatment	RESULTS		Vagina	Fig.
			Uteri			
			Macroscop. Appearance	Histological Findings		
1	3 rabbits 2 inj. 1 contr.	8 days after BOE 1 ml. HS i.v. d.×6	S+ Hyp+ LMuF. D++	Hyp++ gl. tub++ Hcol.		
2	2 rabbits 1 inj. 1 contr.	8 days after BOE 2 ml. HS i.v. a.d.×3	S+ Hyp+ LMuF D+	Hyp+++ gl. tub+ Hcol. Musc+		
3	7 mice 5 inj. 2 contr.	6 days after BOE 0.2 ml. HS s.c. d×10	S+ Hyp+ D+	Hyp+ gl. tub+	At the start : dry After 3rd injection : moist, containing a stringy mucous No oestrus smears obtained	
4	3 rabbits 2 inj. 1 contr.	24 hours after BOE 1 ml. HS i.v. a.d.×8	S+ Hyp++ LMuF D++	Hyp+ Ed+ gl. tub+++ Hcol. V. Musc+++		3,3C 4,4C
5	3 rabbits 2 inj. 1 contr.	2 weeks after BOE 1 ml.HS i.v. a.d.×8	S+ Hyp++ LMuF D++	Hyp++ Ed+ gl. tub++ Hcol. Musc+++		

logical examination showed no difference between the uterine walls of treated and untreated animals. (2) Out of 15 litters of fully-grown spayed rabbits 4 responded with uterine growth and hypertrophy of the mucosa, 6 showed only an increase in length of the uterine horns, and the remaining 5 did not differ from their respective controls.

III. *Preliminary experiments upon the nature of the action of semen injection.*

The microscopical appearance of, and in particular the histological findings in, some of the uteri of the does which had been subjected to semen injections were suggestive of progestational changes. In order to establish whether the injected sperm itself possessed any progestational activity, we assayed the effect of semen injections on spayed rabbits primed with stilboestrol. No difference was noticed between the does

D

which had received stilboestrol only and those which after the stilboestrol treatment had been injected with human semen. The results of these experiments were uniform although we used varying amounts of stilboestrol for the priming treatment and more recently substituted boar's sperm or freshly-collected rabbit's sperm for the human semen in the test-injections.

We have performed a few experiments in order to establish whether the action of semen is affected by heat. We pooled the semen of several donors and kept half the quantity in a boiling water bath for 15 minutes. The heated and the untreated semen were injected into different does of the same litter. Whereas a positive result was obtained with the unaltered specimen, the heated portion proved to be inactive.

In view of the fact that heating causes an insoluble protein precipitate to be formed in the seminal fluid the result of these experiments allows of two explana-

tions, viz. either the active principle itself is thermolabile or it is absorbed and engulfed by proteins which are being rendered insoluble by heating.

Finally we investigated the effect of acetone on the semen. We poured pooled semen into 5 times its volume of acetone, and immediately thereafter we separated the acetone soluble fraction from the precipitate. The acetone was evaporated *in vacuo* (at about 37°C). The acetone soluble residue was emulsified in saline whereas the acetone precipitate was thoroughly ground and suspended in acidified saline (pH5). In no instance have we seen the acetone soluble portion to have any action upon the genitalia; whereas the acetone precipitate was potent when obtained from active semen. It would appear, therefore, that the active principle in semen is precipitated by acetone together with its protein-fraction. Whether it is itself a protein or a protein derivative or an acetone insoluble lipid must be determined by further experiment.

In view of the fact that the volume of one human ejaculate is comparatively small and that pooling of different samples of unknown activity might confuse the issue, we decided to use animal semen, and in particular boar's semen, which is voided in quantities of several hundred ml. at a time.

We are greatly obliged to Dr. A. Walton of the Animal Research Station, Cambridge, for kindly supplying us with boar's sperm in 1944. We divided the large amount of one ejaculate into smaller portions and kept them in a frozen state. Prior to any single experiment the material needed was thawed and the rest left untouched. One hundred ml. of boar's sperm were slowly poured during constant stirring into 400 ml. of acetone. The precipitate was quickly separated from the supernatant fluid, dried *in vacuo* at low temperature and then extracted with 200 ml. of benzene. After 24 hours the benzene was replaced by another 200 ml. of fresh benzene. Twenty-four hours later the 2 batches of extract were pooled, filtered and made up again to 400 ml. with benzene. Of this, 100 ml. were evaporated and the residue dissolved in 10 ml. of pure olive oil. Two immature rabbits of a litter of 3 received intramuscular injections of 2 ml. of this oily solution on 2 subsequent days. Forty-eight hours after the second injection the 3 litter mates were killed. At autopsy the ovaries of the injected does were found to be much larger than were those of the control rabbit. Striking was the difference in the appearance of the uteri. The control was pale and thread-like, whereas the uteri of the injected animals appeared dark red, large and coiled. Their lumen was distended and filled with a stiff mucus. Histological examination revealed the presence of numerous mature as well as ripening follicles in the ovaries. The uterine vessels were engorged, the diameter of the uterine mucosa was about twice that of the control. Glandular tubules were abundant but there was no sign of secretion. The endometrial lining consisted of large darkly-stained cuboidal cells without vacuoles.

Another 200 ml. of the benzene extract were poured with constant stirring into 800 ml. of acetone. The resulting white precipitate was collected on a dense filter and redissolved in 20 ml. benzene. The clear benzene solution was put on an electric water bath and, when almost evaporated, 10 ml. saline were added. This emulsion was tested on 2 immature does. The result was identical with that just described as a sequelae of the injection of the unprecipitated benzene extract.

These experiments suggest that the effect of semen injection is entirely, or at least partly, due to one or more factors which are insoluble in acetone but soluble in benzene.

INSEMINATION.

Although insemination would appear to be the ideal method of reproducing physiological conditions, it must be realized that such a means is fraught with many difficulties and fallacies. For instance, manipulation of the rodent· vagina may produce ovulation (rabbit, ferret) or pseudo-cyesis or both. For this reason we used only spayed rabbits and guinea-pigs for our insemination experiments. After prolonged and intensive treatment we have observed hyperaemia and increase in size of the uteri, glandular proliferation and cell infiltration in the uterine mucosa; the epithelial lining of the mucosa consisting in 2 or 3 layers of large cuboidal cells, many of which contained vacuoles. But in spite of this we are reluctant to draw any conclusions from these experiments as similar results were obtained with boiled semen, which, when injected intravenously, had proved to be inactive. It remains to be seen whether the inactivation of semen by heat is a reversible process. If so, the results of insemination with heated sperm would not only be explained but would even *a fortiori* prove the effectiveness of semen absorption through a mucous membrane. In order to clear this problem we intend to continue insemination experiments on hypophysectomized rabbits and it is to be hoped that fresh experiments will be undertaken on these lines in South Africa where baboons are readily procurable and the results can be checked and followed up.

HOMOLOGOUS SEMEN.

Although experimentation with fresh boar's sperm is a protection against certain fallacies connected with the use of semen from sterility clinics we realized that the necessity of keeping the material frozen for several days or even weeks involved the risk of deterioration of the substance. We came, therefore, to the conclusion that it was preferable to use fresh rabbit sperm from our own animals which was obtainable at any time desired in the course of our experiments. Moreover, since for obvious reasons it is preferable to avoid the introduction of foreign protein, we confined ourselves to experiments with rabbits.

The first series of experiments with rabbit semen was carried out on 12 litters of does using the same technique as we used in our experiments with human sperm. In 8 of these 12 assays the injection of homologous sperm had a definite influence on the reproductive apparatus of the rabbits (see Table III). Figs. 5, 5a and 5b illustrate the effect on an ovary and a uterine horn of a 7-weeks-old doe. Follicle-stimulation and precocious development of the uterus were brought about by 3 intravenous injections of 0.8 ml. of freshly collected rabbit sperm. In Fig. 6 we see that the semen injections have not only warded off the effect of spaying on the uterus, but have produced marked hypertrophy. In contrast to such findings are the results of other experiments of which Fig 7 shows a typical example. There we see that the injections have caused the uterine horn to grow longer but there was no difference in the width of the horns of the control animal on one side and of the injected doe on the other.

Admittedly it is extremely difficult to assess results in border-line cases by roughly measuring the uterine horns of 2 different rabbits even though they are litter mates; but these border-line cases are of great interest and importance from the human clinical standpoint, in that the growth of the immature uterine horns is analogous to the development seen to occur in the hypoplastic uteri of women after weeks or months of marriage. In order to eliminate as far as possible this source of error and obtain an objective yardstick for the assessment of results, we devised the

TABLE III

No.	Age and Size of Litter	Prior to Semen Inject. Time	Actual Experiment	Ovaries Macrosc. Appear.	Ovaries Histolog. Findings	Uteri Macroscop. Appearance	Uteri Histolog. Findings	Fig.
1	3 rabbits	48 hours BOE	(1) 0.5 ml. HoS i.v. a.d.×8 (2)			S++ Hyp++ + LMuF	Hyp++ Ed++ Hcol.+ gl. tub.+ Musc.+	
	5 months		(3) 0.5 ml. saline i.v. a.d.×8 contr.			Thin, pale	BA	
2	2 rabbits	3 weeks BOE	(1) 0.8 ml. HoS i.v. d.×3	S+	FoM Lut+	S++ Hyp+ LMuF	Hyp+ Musc.++ Hcol c++	5, 5A, 5B
	7 weeks		(2) 0.8 ml. saline i.v. d.×3 contr.		immature	thin, pale	NAD	
3	2 rabbits	3 weeks BOE	(1) 0.7ml. HoS i.v. a.d.×8			L++ thin, pale	not examined	7
	3 months		(2) 0.7 ml. saline i.v. a.d.×8 contr.			pale	not examined	
4	2 rabbits	1 week BOE	(1) 1 ml. HoS i.v. a.d.×3			S++ Hyp+++	not examined	6
	4 months		(2) 1 ml. saline i.v. a.d.×3 contr.			pink	not examined	
5	2 rabbits		(1) 0.5 ml. HoS i.v. d.×8	S+	FoM+R Lut 0	S+ Hyp+ LMuF	Hyp+ gl. tub++ Hcol.+Musc.+	
	7 weeks		(2) 0.5 ml. saline i.v. d.×8 contr.		immature	thin pale	not examined	
6	3 rabbits		(1) 0.8ml. HoS i.v. d.×8 (2)	S±	FoM+ Lut 0	L+ thin, pale	NAD	
	9 weeks		(3) 0.8 ml. saline i.v. c.×8 contr.		immature	thin, pale	not examined	
7	2 rabbits		(1) 0.7 ml. HoS i.v. d.×8	S±	FoM+R Lut 0	L+ thin, pale	Musc.+	
	8 weeks		(2) 0.7 ml. saline i.v. c.×8 contr.		immature	thin, pale	NAD	
8	2 rabbits		(1) 0.7 ml. HoS i.v. d.×6	S±	as control	L++ thin pale	as control	
	9 weeks		(2) 0.7 ml. saline i.v. c.×6 contr.	NAD	NAD	thin, pale	NAD	

following technique for further experiments. When unspayed animals were used, we removed the ovary and the whole uterine horn of one side 24 hours before starting with the actual assay, making sure at the time of laparotomy that the other ovary and horn were not longer or larger than the amputated organs. The latter were preserved in Bouin's solution. Twenty-four to thirty-six hours after the last injection the does were killed and at the necropsy the corporate ovary and uterine horn were carefully dissected out and also placed in Bouin's fluid. A few days later, when well fixed, the two ovaries and horns were compared.

Bearing in mind that during the days of experimentation a certain amount of growth is physiological, we used a litter mate as a control, subjecting it to the same operation but not to any seminal fluid injection. This enabled us to estimate how much the increase in the size of the organs of the experimental animals was physiological and how much due to the injections.

Twelve experiments on unspayed litters were carried out with this technique (see Table IV). In 3 there were no definite differences between the ovary and the uterus removed before and after the injection. Six of the remaining 9 litters were immature. The ovarian response to injections of homologous semen in these animals was either generalized follicular stimulation or maturation of a very few follicles with simultaneous retardation of the remainder as will be seen in Figs. 8 and 9, which picture the ovary of an 8-weeks-old rabbit which was subjected to such an experiment. Such stimulation and retardation of the follicles is an interesting feature deserving further investigation. Noble (1939) made a similar observation in immature rats after prolonged treatment with testosterone proportionate injections and we also made note of this result in our earlier experiments with human semen (*vide* page 328).

The above technique proved especially helpful in assessing the effects upon the uteri. All the horns removed at the end of the experiments had considerably increased in length as compared with the corresponding horns amputated before the first injection (*vide* Fig. 10). In some experiments we found that the horns had also increased in width and in these histological changes were observed similar to those described above.

Fig. 11 is a photograph of the uterine horns and ovaries of 3 litter-mate does. "S" was injected with untreated sperm; "CB" with boiled sperm and "CN" with normal saline.

The ovaries of "S" differ in size, the left one being larger than the control; the comparison of the two horns is interesting, for whereas there is no difference in their width, both being thread-like, the left horn had grown to more than double the length of the right.

The injection of boiled semen (CB) had no effect on the size of the ovary but it is noteworthy that the right uterine horn which was amputated prior to the injections was found to be larger than the left one. Moreover, the amputated ovary of the control doe (CN) was larger than the corresponding organ observed at autopsy. Besides, it will be seen that the corpora uteri and vaginae of the does "CB" and "S" are much thicker than the corpus of the control doe "CN". We have noted these facts without being able to offer an explanation.

Finally, we have to report the results of 16 experiments on spayed litters using this technique. Five of these were negative. The most interesting conclusion, which we have drawn from the remaining 11 assays, is that semen injections were able to prevent those atrophic changes that take place after

TABLE IV.—UNSPAYED ANIMALS

Age and Size No. of Litter	Treatment		Results				
	Prior to Semen Inj. Time	Actual Experiments	Ovaries		Uterus		Fig.
			Macroscop. Appearance	Histolog. Findings	Macroscop. Appearance	Histolog. Findings	
1 2 rabbits	24 hrs.: LOE+LHE	(1) 0.8 ml. HoS i.v. d.×7	RO=LO	RO: FoM+R	RH: S++ Hyp+	RH: Hyp++ Hcol+ gl. tub++ Musc++	8+ 9
8 weeks		(2) 0.8 ml saline i.v. d.×7 contr.	small	immature ovary	white, thin RH=LH	NAD	
2 4 rabbits	24 hrs. LOE+LHE	(1)	RO LO	FoM±	RH: LH=65:39 S+	Hyp+ Hcol.	
		(2) 0.8 ml. HoS i.v. d.×5	RO=LO	FoM+R	RH: LH=58:32 S+	gl. tub+	
9 weeks		(3)	RO LO	FoM+R	RH: LH=62:33 S+	Musc++	
		(4) 0.8 ml. saline i.v. d×5 contr.	RO=LO	RO=LO	thin, small R:L=41:37	RH=LH	
3 2 rabbits	24 hrs. ROE+RHE	(1) 1 ml. HoS i.v. a.d.×8	LO: Cy	LO: Hyp++	LH: RH=130:95	NAD Hyp+	
1 year		(2) 1 ml. saline i.v. a.d.×8 contr.	RO=LO	RO=LO	LH: RH	NAD	
4 2 rabbits	24 hrs. LOE+LHE	(1) 0.8 ml. HoS i.v. a.d.×5	RO=LO	RO: Hyp+ FoM+R	RH: LH=85:55 L+	NAD	
2 months		(2) 1 ml. saline i.v. a.d. × 5 contr.	RO=LO	RO=LO	RH: LH=60:52	NAD	
5 2 rabbits	24 hrs. LOE+LHE	(1) 1 ml. HoS i.v. a.d.×4	RO: S+	Not examined	RH: Hyp+ L+	Not examined	10
2 months		(2) 1 ml. saline i.v. a.d.×4 contr.	-RO=LO	not examined		not examined	

TABLE IV. (Continued)

No.	Age and Size of Litter	Treatment		Results				
		Prior to Semen Inj. Time	Actual Experiments	Ovaries		Uterus		Fig.
				Macroscop. Appearance	Histolog. Findings	Macroscop. Appearance	Histolog. Findings	
6	3 rabbits 2 months	24 hrs. LOE+LHE	(1) 0.8 ml. HoS i.v. d.×6	LO larger RO	not examined	LH longer but not larger than RH	not examined	11
			(2) 0.8 ml htd. HoS i.v. d.×6	RO=LO	not examined	RH thicker than LH	not examined	
			(3) 0.8 ml. saline i.v. d.×6 contr.	RO larger LO	not examined	LH=RH	not examined	
7	2 rabbits 8 months	24 hrs. ROE+RHE	(1) 1 ml. HoS i.v. d.×10	LO : Cy+	LO=RO	LH : RH=105 : 80	LH : Hyp+ gl. tub+	
			(2) 1 ml. saline i.v. d.×10 contr.	LO=RO	LO=RO	LH : RH=87 : 76	LH=RH	
8	2 rabbits 10 mths.	24 hrs. LOE+LHE	(1) 1 ml. HoS i.v. a.d.×8	RO=LO	RO=LO	RH : L+ RH : LH=75 : 58	RH=LH	
			(2) 1 ml. saline i.v. a.d.×8 contr.	RO=LO	RO=LO	RH : LH=69 : 63	RH=LH	
9	2 rabbits 2 months	24 hrs. ROE+RHE	(1) 0.8 ml. HoS i.v. d.×7	LO : S+	FoM+ Lut+	LH : S+ RH : LH=35 : 60	LH : Hcol+ Musc++ gl. tub+	
			(2) 0.8 ml. saline i.v. d.×7 contr.	LO=RO	LO=RO	RH : LH=37 : 48	RH=LH	

TABLE V.—SPAYED ANIMALS

No.	Age and Size of Litter	Treatment — Prior to Semen Inj. Time	Treatment — Actual Experiments	Uterus — Macroscopical Appearance	Uterus — Histological Findings	Fig.
1	2 rabbits 10 mths.	24 hrs. : BOE+LHE	(1) 0.7 ml. HoS i.v. a.d. ×10	RH : LH=84 : 69 L+ thin pale	NAD	
			(2) 0.7 ml. saline i.v. a.d. ×10 contr.	RH : LH=48 : 61	BA in RH	
2	3 rabbits 6 months	2 weeks BOE	(1) 0.8 ml. HoS i.v. d. ×8	LH : RH=67 : 48 S++ Hyp+	LH : Hyp++ Hcol gl. tub+	
			(2) 0.8 ml. HoS i.v. d. ×8	LH : RH=70 : 59 S+	LH : Hyp+	
		24 hrs. RHE	(3) 0.8 ml. saline i.v. d. ×8 contr.	LH : RH=42 : 54 thread like	BA	
3	2 rabbits 8 months	4 weeks BOE	(1) 1 ml. HoS i.v. a.d. ×7	LH : S+++ Hyp+++ D+++ S+ LMuF	LH : Hyp++ cub+++V gl. tub++ Musc++	12
		24 hrs. RHE	(2) 1 ml. saline i.v. a.d. ×7 contr.	LH=RH thin, white S—	LH=RH atrophic	
4	2 rabbits 8 months	4 weeks BOE	(1) 0.6 ml. HoS i.v. a.d. ×8	LH : S+ Hyp++ LMuF LH : RH=58 :29	LH : Hyp+ cub. gl. tub++ Musc++	
		24 hrs. RHE	(2) 0.6 ml. saline i.v. a.d. ×8 contr.	thin, pale S— LH : RH=34:30	BA	
5	2 rabbits 3 months	24 hrs. BOE+RHE	(1) 0.8 ml. HoS i.v. a.d. ×8	LH : S++ Hyp+ D+++ LMuF	LH : Hyp+ Ed+++ gl. tub++ Musc++	
			(2) 0.8 ml. saline i.v. a.d. ×8 contr.	thin, pale	NAD	

TABLE V. (*Continued*)

No.	Age and Size of Litter	Treatment		Macroscopical Appearance	Uterus		Fig.
		Prior to Semen Inj. Time	Actual Experiments		Macroscopical Appearance	Histological Findings	
6	2 rabbits 7 weeks	24 hrs. BOE+LHE	(1) 0.6 ml. HoS i.v. a.d.×9	L+	RH:LH=63:38	RH : Hyp+ Musc+	
			(2) 0.6 ml. saline i.v. a.d.×9 contr.	pale, thin	RH:LH=32:36	RH : BA	
7	2 rabbits 10 weeks	24 hrs. BOE+RHE	(1) 0.7 ml. HoS i.v. d.×7	LH : L+	RH:LH=38:59	NAD Musc+	
			(2) 0.7 ml. saline i.v. d.x.7 contr.	L—	RH:LH=33:39	NAD	
8	2 rabbits 6 weeks	24 hrs. BOE+RHE	(1) 0.5 ml. HoS i.v. a.d.×8	LH : L++	RH:LH=24:52	NAD	
			(2) 0.5 ml. saline i.v. a.d.×8 contr.	LH : thread like L—	RH:LH=26:20	LH : BA	
9	2 rabbits 4 months	1 week BOE 24 hrs. RHE	(1) 0.9 ml. HoS i.v. d.×8	LH : S++ Hyp+		not examined	13
			(2) 0.9 ml. saline i.v. d.×8 contr.	LH=RH		not examined	
10	2 rabbits 10 weeks	2 weeks BOE 24 hrs. LHE	(1) 0.8 ml. HoS i.v. a.d.×7	RH : L+	RH:LH=53:30	RH : H col gl. tub+	
			(2) 0.8 ml. saline i.v. a.d.×7 contr.	RH : S—	RH:LH=30:35	RH : BA	
11	2 rabbits 7 weeks	24 hrs. BOE+LHE	(1) 0.7 ml. HoS i.v. a.d.×8	RH : L+	RH:LH=62:39	RH : Musc+	
			(2) 0.7 ml. saline i.v. a.d.×8 contr.	RH : L—	RH:LH=25:35	RH : BA	

castration. Moreover, regrowth in the remaining horn of a uterus which had already shown atrophic changes has been observed. Figs. 12 and 13 illustrate this fact. On the other hand it will be seen from Table V that the reaction of the uteri of spayed does to semen injections mostly consisted only in an increase in length.

DISCUSSION.

First it is necessary to focus attention on those experiments which gave positive results:

1. The ovarian response of immature animals to semen injections can be grouped in two ways, namely, those in which the semen injections were followed by follicle stimulation leading to the well-known histological picture of an ovary studded with mature or almost mature follicles. These ovaries were usually much larger than their respective controls. In the second group the ovaries not only failed to increase in size but were even smaller than the controls, the histological section revealing a picture characterized by the presence of a few large follicles side by side with small ones. This obviously suggests a dual effect—viz. stimulation of a few follicles and retardation in the development of others. Noble made a similar observation in immature rats treated with testosterone proportionate injections. It may be tempting to interpret our findings likewise as a testosterone effect. We are, however, reluctant to do so because it is not known how much testosterone or similarly-acting substances are contained in the injected semen. This question must be left in abeyance until more is known about the principle or principles responsible for the effects of semen injections, for it should be borne in mind that semen is a complex fluid consisting of the secretions of the testis, the seminal vesicles and the prostate. It is very probable that such a material contains several active substances which may influence one another either in a synergistic or antagonistic or even in a complementary way.

2. The uterine response of the spayed and unspayed mature and immature animals consisted in an almost uniform increase in length, although the reaction of the mucosa seemed to vary to some extent with the presence or absence of the ovaries. This observation suggests that the semen injections act directly on the myometrium; it appears, however, that the effect on the mucosa depends also upon other factors.

Bachsich, Sharman and Wyburn (1945) found in their otherwise negative experiments with semen from " sterility " clinics a slight uterine hypertrophy in immature guinea-pigs after parenteral seminal injections. They did not regard this as significant. We cannot follow them because to us this effect on an immature uterus is of the greatest importance, in that the basis on which our experiments rest is the clinical finding that the immature uteri of virginal women start to grow under the influence of regular sex life. It may also be recalled that Deanesly and Parkes (1937) found the size of the uteri to have increased after treatment with testosterone. It is suggestive to interpret such maturation as being the effect of some substance in the semen because uterine hypoplasia in young women is commonly associated with non-ovulation or, at least, immaturity of the ova. Moreover, it will be recognized that such women begin then to menstruate regularly, whereas formerly their cycles were indeterminate, suggesting that semen contains a complementary factor to an ovarian amboceptor enabling the uterine mucous membrane to act as a receptor.

Such a hypothesis is not necessarily contradicted by the fact that we often failed to demonstrate any ovarian response in our experiments when uterine growth was

noted, for it must be recalled that the ovaries are under the constant influence of the anterior pituitary which may enhance or inhibit the effect of any exogenous stimulus. It is not without interest to recall that in certain Eastern countries young women start having regular intercourse with their husbands directly after the first menstrual period has occurred (10 to 13 years). It is, however, a thing of great rarity for conception to take place within a year or more of married life, which would suggest that maturation of the ovary and uterus is stimulated and completed by the absorbed semen.

The variety of ovarian and uterine changes following semen injections suggests that the results depend not only on the nature of the injected material but also to a similar extent on the phase of the receptor organ. This may explain why 30 per cent of our experiments were failures even when freshly-collected homologous semen was employed.

The part which the ovary and the pituitary play in uterine development is now well established; the action of the adrenals, however, is not so well defined although there is no doubt that androgens of cortical origin exercise an influence on the female genitalia. It is, therefore, assumed that the effect of semen injections on the uterus will not only depend on the nature and the quantity of the active principles in the introduced material but also on simultaneous hormonal influences from the ovaries, the pituitary and the adrenals.

In order to analyze the mode of action it will, therefore, be necessary

(a) To use animals in which the hypophysis, the adrenals or both have been removed.

(b) To isolate the active principles and establish the action of such on spayed and unspayed immature animals.

(c) It is suggested that similar experiments be carried out on baboons, because the generative cycle in primates is the same as that in homo sapiens, whereas the cycle in lower animals is not comparable to that seen in man.

SUMMARY.

1. Semen injections have a follicle stimulating effect upon the ovaries of immature animals; sometimes such injections have a dual effect, viz. stimulation of a few and retardation of many follicles.

2. Seminal injections cause uterine horns to grow in length and in some instances also glandular hyperplasia and oedema of the uterine mucosa are observed.

3. Positive results were obtained in 53 per cent when human semen from Sterility Clinics was used, while freshly-collected homologous animal sperm yielded 70 per cent of positive results.

4. The results of insemination were inconclusive. Reasons are submitted.

5. Attempts have been made to extract and precipitate the active principle or principles in semen.

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The Rh Factor in Obstetrics

BY

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Interest in the Rh factor has greatly increased during the past few years, especially since the establishment of its role in intragroup transfusion reactions and haemolytic disease of the newborn (Levine *et al.*, 1941; Boorman, Dodd and Mollison, 1942; Race *et al.*, 1943). There seems little doubt that Rh incompatibility between mother and foetus plays a decisive role in certain foetal conditions now grouped under the term " haemolytic disease of the newborn." Since the aetiology of a large group of pathological conditions in obstetrics in still unknown, various authors have attempted to relate many of these conditions to Rh and other antigenic incompatibility between mother and foetus. Quigley (1945) and others suggested that a possible connexion exists between blood-incompatibility in husband and wife and habitual abortion. Schwartz and Levine (1943) point to the importance of the Rh factor in cases of late abortion. Its possible relation to toxaemia of pregnancy has also been suggested (Javert, 1942). In an extensive study on the importance of the Rh factor in various obstetric conditions, Harrison and Meacock (1945) have not found evidence to suggest any connexion between the Rh factor and abortion, toxaemia of pregnancy and a number of foetal conditions other than those due to haemolytic disease of the newborn.

During the past 3 years we have studied the relation between the Rh factor and several groups of pathological conditions in obstetrics. The results of these studies will be reported below : —

Material and Methods.

Sterile samples of blood for Rh determination and detection of Rh antibodies were taken from 244 women suffering from various obstetric conditions. The tests were performed as follows : A 2 per cent suspension from the blood clot, after removal of the serum, was prepared in normal saline. A drop of this suspension was added to a drop of Rh test serum and incubated in a water bath at 37°C. for one hour. Results were then read macroscopically and microscopically. The test sera used were those of Rh_0 antiserum* and human Rh_0 antisera obtained from patients. At the beginning of this study only anti Rh_0 sera were available. Later on the determinations were performed with 3 anti Rh sera (Rh_0, Rh′, Rh″). In all Rh negative cases, the patients' husbands' typing was also performed, and in part of the cases the Rh factor of the children was studied. The sera of the Rh negative women were tested for Rh antibodies. At first, only the agglutination test was performed; later on, however, the " blocking " as well as

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* Obtained from Certified Blood Donor Service, Jamaica, N.Y.

"conglutination" reactions were performed.

The technique employed for the agglutinating, blocking and conglutinating methods were those described by Wiener (1945).

In the evaluation of the role played by the Rh factor in any disease-group, 2 elements were considered: the rate of the Rh negative women among those affected, and the detection of Rh antibodies in them.

In a previous study we have found that the rate of Rh negative women in our community is 9.6 per cent (Gurevitch, Brzezinsky and Polishuk, 1947).

I. *The Role of the Rh Factor in the termination of pregnancy during the first 28 weeks (i.e. abortion).*

(a) *Habitual abortion.* For the purpose of this study a diagnosis of habitual abortion was assigned only for cases in which at least 3 consecutive abortions have occurred and in which no previous pregnancy had lasted longer than 28 weeks. Cases in which anatomical or general disorders were found, and could account for the abortions, have been excluded from this study. In all cases syphilis was excluded by the Wassermann and Kahn tests in both husband and wife. We have studied a total of 41 cases of habitual abortion and have found among them only 3 Rh negative women, a rate of 7.3 per cent (Table I).

(b) *Other forms of abortion.* This group includes cases of repeated abortions, single abortions and missed abortions. Under the term "repeated abortion" are included women who had 2 abortions, or more than 2 abortions with at least 1 normal delivery. Cases in which a definite cause (anatomical or general) for abortion was found have been excluded. The results of determinations of the Rh factor in these cases are reported below in Table I.

TABLE I

Clinical diagnosis	No. of cases	Rh negative	Percentage	Rh positive	Percentage
Habitual abortion	41	3	7.3	38	92.7
Repeated abortion	22	1	4.5	21	95.5
Single abortion	59	6	10.2	53	89.8
Missed abortion	12	2	16.6	10	83.4
	134	12	8.9	122	91.1

As can be seen from Table I, the incidence of Rh negative women in all the forms of abortion does not exceed that found in the population at random. The number of cases of "missed abortion" is too small to permit any conclusions in this respect. Rh antibodies were not detected in the Rh negative cases. This fact coupled with the low incidence of Rh negative women in this group permits the conclusion that no relation exists between Rh incompatibility and abortion.

A characteristic case of repeated abortion which on clinical grounds alone would be suspected of Rh incompatibility is reported below:

Mrs. A. L., aged 32. Her past obstetric history is as follows: The first pregnancy (1939) terminated with the delivery of a male child at term. Her second pregnancy (1941) ended with a stillbirth at the 8th month. The patient's subsequent 3 pregnancies (1942, 1943, 1945) ended in spontaneous abortions in the 2nd and 3rd months. General and gynaecological examinations revealed no cause for the repeated abortions. Blood chemistry was normal. Blood typing revealed the patient to be ARh_1 and her husband ORh_1. Wassermann and Kahn examinations were negative. No antibodies were found in the patient's blood. In this case the normal delivery followed by an unexplained stillbirth and 3 consecutive abortions gave rise to the suspicion that Rh incompatibility played a role in the aetiology. The haematological findings, however, did not confirm this suspicion.

II. *Foetal Pathology in the last Trimester of Pregnancy.*

This group includes cases of stillbirths, macerated foetuses and premature deliveries in which no apparent cause for the condition could be determined. It is to be stressed that toxaemia of pregnancy, diabetes, syphilis and other general conditions were excluded from this group of cases. In Table II we have reported the Rh distribution in this group.

TABLE II.

Diagnosis		No. of cases	Rh negative	Percentage	Rh positive	Percentage
Stillbirths	...	15	2	13.3	13	86.7
Maceration	...	10	1	10.0	9	90.0
Prematurity	...	23	2	8.6	21	91.4
Total	...	48	5	10.4	43	89.6

Rh antibodies in the maternal blood were not detected in any case examined from 6 to 20 days postpartum. It is, therefore, apparent that the stillbirths, maceration and premature deliveries were not due to incompatibility in the Rh factor of mother and child. Some of these 48 cases, a group of 22, presented an obstetric history characteristic of that observed in haemolytic disease of the newborn. These are discussed separately below.

III. *Toxaemias of Pregnancy.*

This group of cases includes hyperemesis gravidarum, toxaemia of pregnancy, pre-eclamptic toxaemia and eclampsia.

Schwartz and Levine (1945), have pointed to the possible relation between pregnancy toxaemias and Rh incompatibility. The results of our findings in these conditions (Table III) point to the lack of any relation between Rh incompatibility and the various forms of pregnancy toxaemia, since the rate of Rh negative mothers is not significantly higher than that found in our population at random, and no Rh antibodies were found in maternal blood taken during pregnancy.

TABLE III.

Diagnosis	No. of cases	Rh negative	Percentage	Rh positive	Percentage
Hyperemesis gravidarum	5	–	–	5	100.0
Toxaémia of pregnancy	28	3	10.7	25	89.3
Pre-eclampsia	6	1	16.6	5	83.4
Eclampsia	2	–	–	2	100.0
Total	41	4	9.7	37	90.3

IV. *Other Pathological Conditions in Pregnancy.*

In this group are included cases of placenta praevia, premature separation of placenta as well as ectopic pregnancy. We have found only 1 case of an Rh negative woman among them. In this case Rh antibodies were not found in the maternal blood 8 days after operation.

TABLE IV.

Diagnosis	No. of cases	Rh negative	Percentage
Placenta praevia	8	–	–
Premature separation of placenta	1	–	–
Ectopic pregnancy	12	1	8.3
Total	21	1	4.8

As would have been expected, there is no relation between these conditions and Rh incompatibility.

V. *The Obstetrical History Characteristic of Rh Incompatibility.*

We have studied a group of 22 cases (see above), who presented a past obstetrical

history characteristic (Levine, *et al.*, 1941; Boorman, Dodd and Mollison, 1942; Cappell, 1946) of that found in foetal disease due to Rh incompatibility. In these cases one or more healthy and living children have been delivered at term, but afterwards either macerated or stillborn children had been born. In some of these cases one or more abortions preceded the present condition. In these 22 cases, only 3 were Rh negative (13 per cent). It should be pointed out that in these 3 cases signs of erythroblastosis foetalis were not found in the children, nor were any signs of iso-immunization found in the mothers. The rate of Rh negative women in this group is slightly higher than that normally observed in our population, but the increase is too low to be of any significance.

The following case is here reported to illustrate the misleading conclusions that may be drawn from the clinical history alone:

Mrs. K. S., aged 35. First pregnancy (1936) ended in spontaneous abortion in the 3rd month. The 2nd and 3rd pregnancies (1937, 1939) ended in the delivery of healthy and living children at term. The 4th pregnancy (1942) terminated by the spontaneous delivery of a stillbirth. Postmortem examination could not be performed In her 5th pregnancy (1944) the patient delivered a premature stillbirth in the 8th month. Blood typing revealed the patient to be ARh$_1$ and her husband BRh$_1$.

Immune antibodies (anti B) could not be detected in the patient's blood. Wassermann and Kahn examinations were negative and blood chemistry was normal. Postmortem examination did not reveal a cause of death.

DISCUSSION.

In this paper we have tried to determine whether Rh incompatibility plays any role in various pathological conditions in obstetrics. The attempt to relate pathological conditions to blood group incom-patibilities of mother and foetus is not new, and dates much earlier than the discovery of the Rh factor. As far back as 1905 Dienst had attempted to explain conditions such as eclampsia or toxaemia of pregnancy on the basis of maternal iso-immunization by foetal blood. Similar attempts have been made in the past by McQuarrie (1923), Ottenberg (1923), and others.

It has been observed that the great majority of cases of haemolytic disease of the newborn occur after delivery or, at most, very near term. This seems to indicate that during pregnancy foetal erythrocytes are protected against the action of maternal immune-antibodies. Such protection seems to wane near term or after delivery. It therefore does not seem probable that Rh incompatibility with maternal immunization may be a cause of termination of pregnancy during the first half of gestation.

Our findings in the first group of cases (Table I) confirm the view (Hunt, 1945; Harrison and Meacock, 1945) that a relation does not exist between habitual abortion and other forms of abortion and the Rh factor.

The possibility that Rh incompatibility may account for some of the unexplained cases of foetal damage (stillbirth, maceration) during the last trimester is naturally great. When the frank cases of erythroblastosis foetalis are excluded (Table II) no increased incidence of Rh negative individuals among women delivered of premature, macerated and stillborn infants is found.

The result of our studies in the third and fourth group of cases (Table III and IV) confirm those of Hurst, Taylor and Wiener (1946) in their recent study on the relation between toxaemia of pregnancy and Rh incompatibility.

Great stress has been laid by various authors on the characteristic pattern of the obstetric history in cases of Rh incompatibility with resultant haemolytic manifestations in the child. In our fifth group of cases, which was selected on the basis of the suggestive obstetric history, we have seen that this does not in itself serve as a diagnostic aid, and is no indication of blood group-incompatibility of mother and offspring.

The results reported here point to one conclusion. Although Rh incompatibility, both theoretically and clinically, must be present in haemolytic disease of the newborn, there is no reason to look upon it as an aetiological factor in the obstetric conditions studied in this paper.

SUMMARY.

1. The incidence of Rh negative women and the presence of Rh antibodies in them has been studied in a group of 244 cases suffering from various obstetric conditions.

2. No relationship could be found between Rh incompatibility and habitual abortion (41 cases), other forms of abortion (93 cases), stillbirths, maceration and premature deliveries (48 cases), and other pathological obstetric conditions (21 cases).

3. The results of our findings in toxaemia of pregnancy (41 cases) point to the lack of any relation between Rh incompatibility and the various forms of pregnancy toxaemia.

4. In a study on 22 cases with an obstetric history characteristic of Rh incompatibility it was found that a suspected obstetric history is no indication of an antigenic incompatibility between husband and wife.

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The Cause of Polar Lie

BY

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IT is the purpose of this article to give an explanation, appealing to reason, for the frequency of vertex presentation and also to suggest a cause for the foetus presenting by the breech in otherwise normal pregnancy.

Until the eighteenth century the Hippocratic teaching that the child lay as a breech until the 7th month and then suddenly underwent a spontaneous version was believed. By the time of Smellie (1750) it was thought that the presentation was maintained throughout pregnancy, but that a few breech presentations turned in late pregnancy. Smellie did much to dissipate this idea. Whitridge William's textbook of obstetrics (1923) gives an excellent account of the theories and development of thought on the subject. In 1861 both Hecker and Schultz showed that it was not really uncommon for the foetus to turn even in the later months. It is now recognized that the lie is variable in the early months, with an increasing inclination to a polar lie · and a vertex presentation as term approaches. The older textbooks contained long arguments as to the aetiology of the vertex lie but most of them were expositions of the various theories that had been advanced, followed by refutations of these arguments. The reader was left unconvinced. For instance Caseaux (1869) concludes his account of the frequency of vertex presentation with " . . . a singular fact which does not seem,

in the present state of our science, capable of elucidation by the material reasons heretofore given." Two theories held sway. For the gravitational theory Matthews Duncan (1868) and Veit (1860) held that a foetus suspended in a fluid tended to sink head first. Schatz in 1900 showed that if the solution was of the same specific gravity as liquor amnii (1.008 to 1.009) the breech end tended to sink. Seitz (1908) countered this by showing that during the last month the head increased in specific gravity and concluded that the force of gravity could account for the frequency of vertex lie. The second theory—the theory of accommodation—was supported by Dubois (1833); Simpson (1848); and Scanzoni (1853), who postulated that the foetus was irritated by the ill fit of breech presentation and moved until it was in the more comfortable fit of a vertex presentation in the uterine ovoid. Modern textbooks tend to skip the arguments and give no explanation. DeLee (1933) mentions " the law of accommodation of Pajot " which states that where an ovoid body lies free in an ovoid container the two long axes tend to become parallel. To call an observed phenomenon a law is not an explanation. Kerr, *et al.* (1944), state that the preponderance of vertex presentations is due to the ovoid foetus, with the head the narrower end, lying in the ovoid uterus wider above. He then states that " it is natural " for the child to take up a permanent position head

down. Why is it natural? He vitiates his argument by adding another reason—that the cranial end of the foetus is heavier. Eden and Holland (1931) give almost the same two reasons but use a slightly better term for an untrue assumption, by saying that the centre of gravity of the foetus lies nearer the cranial end. Ten Teachers (1931) simply state that the foetus "fits best" as a vertex. Gibberd (1938) writes that " the relatively restricted space in the uterus accounts for the frequency with which a longitudinal lie occurs."

Really thoughtful experiments and arguments were published in this Journal by Griffith in 1915. He put forward that an immersed body in fluid of less specific gravity tended to lie with its metacentre or centre of buoyancy vertically above its centre of gravity. The metacentre is the centre of gravity of the displaced fluid. By careful experiments he found that in 7 foetuses near full time the centre of gravity was nearer the breech end than the vertex and that the metacentre in the 2 foetuses he measured was 0.5 cm. nearer still to the breech end. A distance of 0.5 cm. in 2 foetuses is hardly sufficient to found a theory. From his measurements he concluded that there would be a tendency for the foetus to lie breech up and showed that the force tending to produce this movement would be a moment of about 1,383 centimetre-grammes. This is a very tiny force and is in fact 1.19 inch-pounds. This moment would diminish rapidly as the foetus turned from a transverse lie and the metacentre came more closely over the centre of gravity. Moreover in women lying in bed this force would not act; departures from the vertex lie are not more common in these. However, this article did dispose of the loose statements that the head end was the heavier end or the foetal centre of gravity was nearer the vertex.

Much greater forces than this are at work. Griffith mentions them but then goes on to develop his argument as to the physics of an immersed body. The 2 factors which I put forward as the most powerful in determining the predominance of vertex presentation are:

1. The kicking of the foetus.
2. The absence of resistance at the fundus of the uterus and its presence at the lower extremity.

The normal foetus in a position of flexion kicks by extending its hips and knees repeatedly, so propelling its breech away from its feet. The effect of this would be for the foetus to dive round and round, were it in a spherical container. The action of arm movements would be much less effective for the arms are weaker, they are folded across the thorax and covered by the knees, and the hands are so near to the centre of gravity that a thrust imparted there would tend to give little turning movement. Up to the seventh month the foetus is in a spherical container, with the result that it turns head over heels many times. As term approaches the uterus becomes broad at the fundus and comparatively narrow at its lower strait. The turning moment is, therefore, more effective when the breech is lowermost. The moment is still more effective from the presence of the pelvic brim below. There is no similar structure above. Put simply, a flexed foetus in the breech position has something to kick against and hence turn it, whereas as a vertex it has a very poor purchase. A foetus in the breech position has only to give a small kick before its feet find something to thrust against, whereas in the vertex position it must kick some inches before it finds a purchase and that is soft uterine and abdominal walls instead of lower segment and bony pelvis. The measure of this moment cannot be told unless the force of the foot thrust of a

foetus is known. By testing with a spring balance it was found that a full-time foetus could kick between 3 and 4 pounds with 1 foot. If both feet kicked together it would kick between 6 and 8 pounds, and this is borne out by the fact that with a kick a new-born baby can almost lift its weight from one's hands, though of course it cannot sustain it. Griffith's measurements showed that the centre of gravity of a full time foetus averaged 6 inches from the breech. A force of 6 pounds applied at a distance of 6 inches means a turning moment of 36 inch-pounds (42,000 centimetre-grammes) compared with the 1.19 inch-pounds (1,400 centimetre-grammes) produced at their maximum by the inert physical forces. Moreover the kicking movements do not lose their power as the foetus turns. Griffith's moment diminishes as the foetus turns until, when the metacentre is above the centre of gravity, it is reduced to zero. The feebleness of Griffith's moment is easily tested by taking a fresh, stillborn foetus and tying it by means of cotton in the normal attitude of flexion. Suspended in a bath of water with its long axis horizontal and then released, it sinks to the bottom. In a bath 2 feet deep the writer was unable to detect any tendency for the head to descend quicker than the breech and the foetus reached the bottom still horizontal. A touch with a finger and the foetus turned end 'for end with ease. In liquor amnii this alleged tendency for the head to descend quicker would be still less, for liquor with its slightly higher specific gravity would offer a little more resistance to turning.

It comes about then that during the first 2 trimesters the foetus turns end for end repeatedly, propelled by its feet. As the uterus assumes its decidedly oval shape during the third trimester foetal kicking will rapidly and easily convert a breech lie into a vertex, but only slowly and with

difficulty convert a vertex into a breech. It follows that the inert vertex will most frequently come to lie in the narrow lower segment over the pelvic brim.

But what of breech presentation? Why do foetuses sometimes present by the breech? Long lists of causes for breech presentation are given in textbooks—contracted pelvis, placenta praevia, tumours, prematurity, multiparity, dead foetus, hydrocephaly and so on. Excluding all these cases there are still large numbers of breech presentations without such causes and the textbooks merely state that there are many cases for which no adequate cause can be found. It is the writer's thesis that the commonest cause of breech presentation is extended legs. Vartan (1940) in an article entitled "Cause of Breech Presentation" recognized extension as most commonly associated with breech lie but attributed this to "splinting" of the foetal body by the legs and hence difficulty in turning inside the uterus. This word "splinting" is frequently used in this connexion but does it really occur? It sounds reasonable, but the knees of a foetus at term are very flexible and extensible. The writer has not noticed any diminution in the mobility of the foetal body produced by extended legs when delivering a foetus in the breech position. It is the writer's opinion that with the legs extended the normal moment applied to the foetus by kicking is absent. Any kicking that does take place will be at the head end of the foetus and would tend to turn it to a breech lie.

In the primigravida the uterus is most perfectly of the ovoid shape. If this thesis is correct, extended legs should lead to breech presentation more certainly in them than in multiparae. As multiparity increases and the uterus becomes less ovoid and more spherical, the number of breech presentations produced by extended legs should be
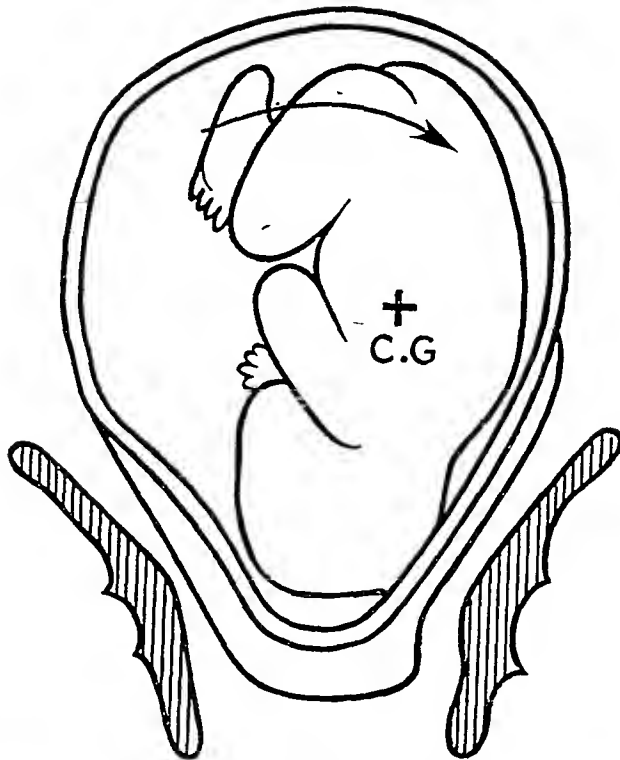
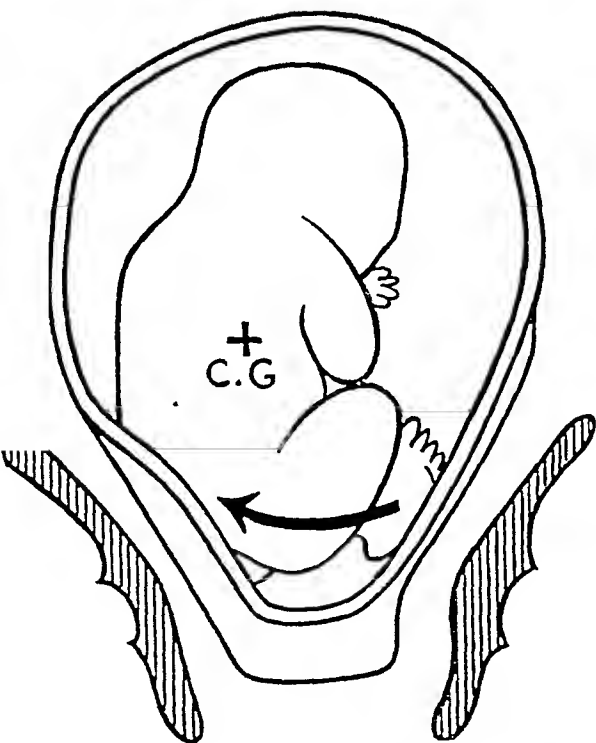DIAGRAM 1. Weak turning moment when the flexed
legs lie at the fundus.

DIAGRAM 2. Powerful turning moment when the
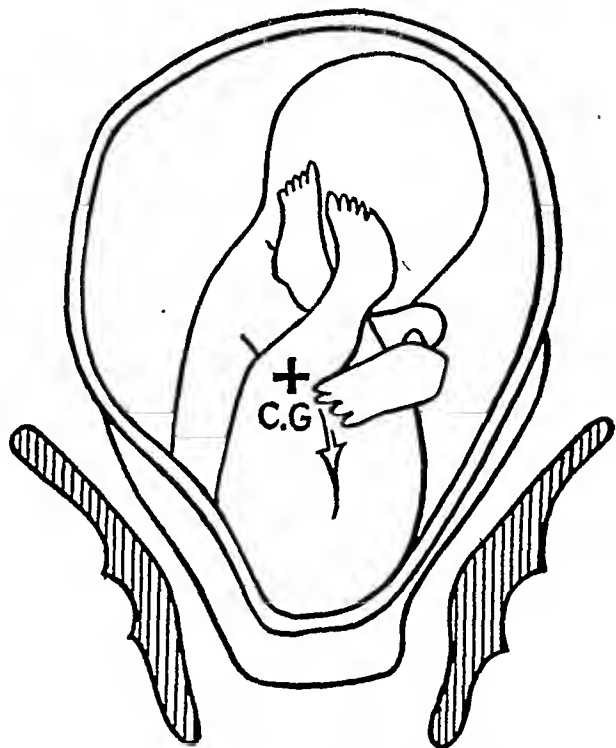flexed legs have the closely applied lower segment
and pelvic walls for purchase.

DIAGRAM 3. With extended legs there is no tendency
to kick away from the breech position.

diluted by the chance occurrence of breech with flexed legs. The foetus in the multigravid uterus is under the same conditions as the foetus before 7 months. For some years the resident obstetric officers at the Princess Mary Maternity Hospital have been urged always to record the state of flexion or extension of the legs in breech presentations, but in spite of this many were merely recorded as " Breech—normal delivery ", " Breech—assisted delivery " and so on. The notes tended to record extended legs only if these demanded any treatment. It is very difficult to find any reliable figures of the incidence of extended legs. Bourne and Williams (1945) state that " in women pregnant for the first time, over 50 per cent of the infants presenting by the podalic extremity have the legs extended ". This true statement conveys an untrue impression. In the figures below, all those cases in which there is no record of the state of the legs are counted as having flexed legs so that the proportion of extended legs is always an underestimate. In the 7 years 1931 to 1937 there were 629 breech deliveries. Of these 309 are excluded because of gross causes for malpresentation such as contracted pelvis, twin, placenta praevia, anencephaly, hydrocephaly, etc. All cases of less than 36 weeks development are excluded.

Parity	Extended legs recorded	Flexed legs or not recorded
0	157	71
1	21	13
2	7	11
3	5	6
4	4	3
5	0	7
6	2	4
7	0	1
8	1	4
9	1	2

In first and second pregnancies extended legs preponderate in the proportion 2 : 1.

After the second child flexed legs preponderate in the proportion 2 : 1. However, because of the failure to record every case fully, these figures are not very reliable.

To supply more accurate figures the X-ray films of all breech cases referred to the radiologist between 1938 and 1945 were scrutinized with the same exclusions as in the other series. The result is more in keeping with one's clinical impression that 90 per cent of breech labours in primigravidae have the foetal legs extended.

Parity	Extended legs	Flexed legs
0	30	3
1	9	1
2	5	1
3	1	1
4	0	1
5	0	0
6	0	0
7	2	0

Teaching on breech presentation usually starts with the complete breech and then considers extended legs as a complication —a " complication " which occurs in over 70 per cent of normal primigravidae with normal foetuses !

CONCLUSIONS.

1. Foetal leg movements tend to turn the foetus end for end.

2. The narrow lower pole of the uterus together with the presence of the pelvic brim makes foetal turning easy of achievement if the legs are flexed with the breech lowermost.

3. The wide, soft, upper pole of the uterus makes turning difficult of achievement if the legs are flexed with the breech uppermost.

4. As a result most foetuses present by the vertex.

5. If the legs are extended the mechanism is reversed and breech presentation is more likely.

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Central Rupture of the Perineum
A Report of a Case with a Review of the Literature

BY

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The birth of a child through the perineum is an unusual occurrence, though by no means excessively rare. The condition is mentioned in almost every textbook of midwifery and the case reports are fairly numerous. There would seem, however, to be a place for a further case report and a full review of such literature on the subject as can at present be traced.

CASE REPORT.

Mrs. D.S. was aged 30. Her first child had been delivered in her own home in 1938. There had been a perineal tear, described by the patient as an "internal tear", which was sutured. Her height was 4 feet 11⅞ inches. Clinical and radiological pelvimetry showed the pelvis to be adequate.

Her second pregnancy was uneventful and she went into labour 7 days after the expected date of delivery. She was admitted to the labour ward of University College Hospital on January 29th, 1946. The first stage of labour lasted 3 hours. A vaginal examination was about to be made when the patient suddenly screamed that the baby was coming. The membranes ruptured and the child's head was seen to be distending the left labium majus. An attempt was made to push the head towards the midline, but this was unsuccessful, owing partly to the strong bearing-down efforts made by the patient. Almost immediately the skin of the labium and the perineum split in several places and a few seconds later the head burst through the skin and was born. The rest of the child followed quickly. The infant was a female, weighing 7 pounds 1½ ounces and was in good condition with only slight head moulding. The length of the child was 20 inches, head circumference

12½ inches, occipito-frontal diameter 5 inches, biparietal diameter 4 inches.

The diagram (Fig. 1) shows the appearance after delivery of the child, with the umbilical cord passing through the tear. There was complete con-
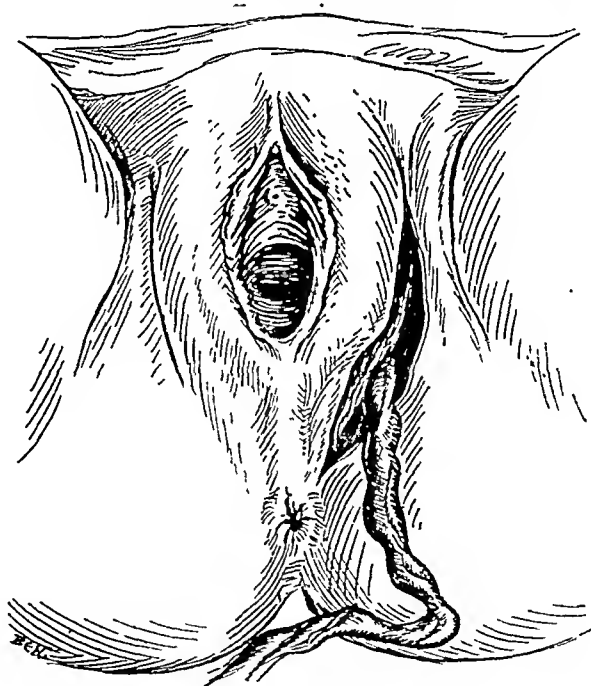

FIG. 1.

Illustrating the vulva and perineum after the birth of the child.

tinuity at the posterior commissure and all round the margins of the vaginal aperture. The fingers could easily be passed through the wound into the vagina, so that the left labium majus lay across the palm of the hand, bridging the gap, and apparently attached only at its anterior and posterior ends. There were also numerous superficial tears of the skin of the vulva and the vaginal

mucous membrane was extensively lacerated, especially on the left lateral wall.

The placenta and membranes were delivered 15 minutes after the birth of the child, through the aperture in the vaginal wall and perineum. There was no uterine haemorrhage, though bleeding from the tear became obvious 1 hour later. The patient did not complain of pain and was surprised to hear that she would have to have stitches inserted.

An injection of papaveretum ("omnopon") and scopolamine was given and an hour later the patient was taken to the operating theatre. She was placed in the lithotomy position and the tissues of the perineum and lower half of the vagina were infiltrated with procaine 0.5 per cent, and adrenaline 1:200,000. The extent of the tear was now carefully examined. It was found that a laceration extended through the skin of the perineum and outer border of the left labium majus along almost the whole of its length. The tear in the vagina was surrounded by much scar tissue and the tissues were extremely friable. The tear extended up the left lateral wall of the vagina almost to the cervix and there were several secondary lacerations in the posterior vaginal wall. There was no significant laceration of the cervix. The perineal body was intact but the left levator ani had been torn through. The rectum and anal canal were intact.

Procedure. The remains of the left labium majus which were bridging the passage between the tear and the vagina were incised for better access. The torn edges of the vaginal wall were brought together with interrupted catgut sutures, after excising as much of the scar tissue as possible. The left levator ani was repaired and the left labium majus was reconstructed. The perineal skin was united. The whole procedure was rendered difficult by the extreme friability of the tissues. The local analgesia was entirely sufficient for the whole procedure. The patient did not complain of pain and seemed unaware of the examination or the insertion of the sutures.

Puerperium. This proceeded uneventfully, except that the superficial part of the tear broke down and became slightly septic. A swab was taken and Pseudomonas Pyocyaneus was grown. Ultraviolet light was given to the perineum twice daily.

On the 14th day it was found on examination that the posterior wall was healed and intact. The perineum had broken down superficially and was gaping slightly but granulating well. It was decided to continue treatment for 3 or 4 days and then to consider resuture. One week later the perineum was almost healed. Resuture was considered unnecessary and the patient was discharged.

Postnatal. The patient attended the postnatal clinic when the child was 5 weeks old. The perineum was almost healed, but slightly deficient. There was no cystocele or rectocele.

One month later healing was complete.

LITERATURE.

A search of the literature has revealed that central rupture of the perineum has been known to obstetricians for many years, though the earliest case reported dates from 1796. No report of a case can be found before that date.

Sir Fielding Ould in his *Treatise of Midwifery* published in 1742 does not mention central rupture of the perineum, though he does give a remarkably clear description of the operation of episiotomy, and indeed of incision of the cervix. Both operations he recommends when cicatrization of the soft parts delays or impedes delivery.

William Smellie (1774) does not describe the condition.

Matthews Duncan (1876) described central tearing or rupture of the perineum but stated that it commonly occurred without a new passage being made into the vagina, a crack appearing in the perineum or vaginal mucous membrane. The complete central rupture with perforation was a rare occurrence. He described 4 cases, but only 2 were true perforating central ruptures.

Baker Brown (1861) reported a case in a paper read before the Obstetrical Society of London in May, 1860. This was the case of a primigravida aged 20 in whom the child was born between the os vaginae and the anus. A hard, constricting band was found

along the posterior margin of the vaginal orifice. The aperture in the centre of the perineum admitted 3 fingers. The posterior vaginal commissure was divided and 2 sutures of iron wire inserted without anaesthesia and apparently without excessive pain to the patient. Complete healing took place. Baker Brown suggested that episiotomy be performed when central rupture of the perineum threatened.

The most complete review of the literature of the subject up to the year 1878 was given by Reeve. This author was able to collect 35 cases from the literature. He gives details of a personal case where he was summoned to a patient who had been delivered of her 3rd child by a midwife. He found an enormous laceration of the perineum, which had divided both sphincters of the anus, but had left the posterior vaginal commissure intact and as thick as a man's thumb. This laceration was repaired with silver wire sutures, but it broke down, and a recto-vaginal fistula remained. An attempt to cure this one year later was unsuccessful. The 35 cases collected by this author were gathered from extensive literature, including the cases described by Matthews Duncan and Baker Brown. The earliest case report that Reeve was able to trace was from Loder who reported the case in 1797, one year after its occurrence. This reference was found by Reeve in Mursinna-Osiander, *Handbuch der Entbindungs*, 1820, ii, 245.

Wilson (1878) described a case where the child was born through the perineum and the placenta through the vagina. The fourchette and sphincter remained intact.

Rogers described a similar case in 1879. This occurred in a primigravida of 24. He gives the reasons for the occurrence of the condition as a contracted state of the vaginal orifice, an inordinately long perineum or possibly a poorly curved sacrum as is found in a pelvis of the male type.

Cunningham (1879) described a remarkable case where the child escaped into the abdominal cavity through a tear in the posterior vaginal wall. Delivery was effected through the rent and *per vaginam* but death of the mother took place on the 3rd day.

Harley (1881) described the case of a primigravida of 25. Hymenectomy had been performed but the husband still complained of difficulty because " that bone " (i.e. the pubes) was still there. The first child was born through the perineum and it seemed that the low pubic arch was forcing the child backwards. A central laceration occurred with one inch of the perineum intact in front and the sphincter ani also intact. In the discussion on Harley's paper Rutherford Kirkpatrick described 2 cases and More Madden 1, all 3 having occurred at the Rotunda Hospital.

Beatty (1882) described the case of a primigravida of 24 where the child was born and the placenta followed through a central rupture which was found to be complete from side to side, but with the vagina and rectum intact.

Ribémont-Dessaignes and Lapage (1894) described the condition as fairly uncommon. They attempt to explain its mechanism on similar lines to those suggested by Rogers and give 4 drawings taken from cases.

Baudry (1894) described a case where the child's hand came out through the anus. It was replaced and the child delivered *per vaginam*. Afterwards it was found that there was a large hole between the vagina and rectum with an intact perineum.

Dodson (1906) described a case in a primigravida of 21. In a precipitate labour the child was born through the perineum, the vagina, rectum and anus remaining intact. The child weighed 6 pounds 12 ounces and after suture of the tear there was a good recovery.

Seyffardt (1922) described a case where the child was born through the perineum, while episiotomy was being considered. It was found that the perineum was torn through to the anus. The rectum was lying free but intact. There was a deep tear in the posterior vaginal wall, exposing the peritoneum. The tear was repaired and recovery was complete in 14 days.

Scheven (1923) described a case in a primigravida of 21. Here the child was born through a rent between the vagina and anus but the rectum remained intact.

Karlin (1927) described a case of central rupture of the perineum and quoted the literature up to the year 1926; all from German sources. He quoted a paper by Hagen (unobtainable) who gave the findings in 39 cases from the literature. These are tabulated as follows:

Age

17–25	16
26–30	13
30–34	2

arity

Primigravidae	27
Under 25 years	16
Over 25 years	9
Multigravidae	8

oft parts

Narrow or rigid vulva	15
Long perineum	25
Hypoplasia of vulva	2
Normal perineum	1
Gaping perineum	4
Scarring of soft parts	6

Pelvis

Narrow pubic arch	8
Contracted pelvis	9
Normal pelvis	7

Presentation

Vertex presentation	21
Vertex with prolapse of limbs ...	3

Contractions

Violent uterine contractions	23

Sachs (1926) while not describing any cases discussed the mechanism of production of central rupture of the perineum. The condition occurs either in nulliparae or in cases where there has been a previous tear of the perineum or an operation. Delivery is sometimes protracted, sometimes precipitate. In one variety the tissues are rigid, a crack occurs in the perineum and the child escapes through the eventual central laceration. Here labour may be long. In a second variety precipitate delivery takes place and the force of the contractions drives the child through the perineum. In a third variety the child's head escapes out of the vagina into the fascial space surrounding it and eventually bursts through the skin of the perineum or the surrounding structures.

Sachs quotes the opinion of Zangemeister who suggested that in these cases the perineum is elongated and the frenulum lies far forward. The vaginal introitus is not in line with the descent of the head which comes to lie on the perineum rather than on the vaginal walls. Over-stretching of the vagina in the long axis and rigidity of the soft parts are contributing factors.

Naylor (1926) described a case in a primigravida of 36. During the second stage of labour a bleeding spot appeared near the anus. Central rupture of the perineum followed and liquor amnii escaped. An episiotomy was immediately performed and a child weighing 9½ pounds delivered. The anal sphincters and rectum were intact.

Bussalay (1927) described a case where a child, placenta, etc., were delivered through the perineum. He ascribes this to malformation of the ostium vulvae and to excessively powerful uterine contractions.

Duthie (1928) gives a clinical note of a case in a primigravida of 37 who was delivered by a midwife. Precipitate delivery took place through a tear in the perineum. The child was not unduly large.

Afterwards a tear 3 inches long was found to the right of the midline, with a large tear in the posterior vaginal wall. The posterior vaginal commissure was intact.

Tindal and MacLennan (1930) reported a case which they described as a "unique case in the history of perineal tears". The baby was born through an extensive perineal tear, involving the posterior and lateral vaginal walls, levator ani and transversus perinei. The anal sphincter was not involved.

Guglielmi (1932) stated that central perineal laceration, though not very frequent, is less rare than is generally supposed. Varying mechanisms are described. The condition should be avoided if possible by prompt episiotomy. He recommends immediate repair.

Meyer (1935) described 2 cases. The first was a patient aged 28 who had had an episiotomy in her previous labour. In the 2nd labour the child was born through the perineum. In the 2nd case the patient was a primigravida of 20. At the height of bearing-down, the recto-vaginal septum split and the child's right foot came through the perineum. The child was born spontaneously. The vulval orifice was intact and the laceration admitted 3 fingers.

Leclerc (1935) described a case in a girl of 19. The whole perineal body was perforated between the vulva and the anus with the posterior commissure intact. He recommends episiotomy and then suture.

Kovacs (1942) described the condition as "paracentral tear of the perineum" and quoted theories of the causation of the condition from various authorities. He mentions von Bigelow, Klein and Stoeckel as ascribing the condition to the fact that in these cases the perineum is too high. According to von Münster and Mandelstamm a narrow outlet is responsible. Stortfeld and Mathei ascribe the condition to a scarred condition of the perineum and

Fergusson and Seidentopf to rigidity from previous tears. Kovacs suggests that these various factors may all play a part. In a series of 16,000 births collected over 10 years, central rupture of the perineum occurred on only 4 occasions, an incidence of 1 in 4,000 labours. The mechanism suggested by Kovacs is that the foetal head comes to lie in the recto-vaginal space and bursts out of it through the perineum. He suggested a congenital origin and illustrates 2 sites where congenital weaknesses of the pelvic floor may exist. One anteriorly in the triangle formed by the bulbo-cavernosus, ischio-cavernosus and transversus perinei, and the other posteriorly, behind the transversus perinei, and in the triangle formed by it with the levator ani and gluteus maximus. An illustration is given of the latter type of pelvic hernia occurring in a woman of 30. Kovacs believes that these herniae are of atavistic origin, resulting in a congenital weakness of the pelvic fasciae and muscles.

Two papers dealing with central rupture of the perineum have appeared but are unobtainable in this country or in the Army Medical Library, Washington, D.C., U.S.A. These were by Tolosa and Pawel (1940) of Brazil, and by Gerinshteyn (1940) of Russia.

Many general descriptions of the condition have appeared, some detailed and illustrated, though in the majority of obstetrical textbooks the subject is dealt with in a few lines and is described as rare or unusual.

Hermann (1910), in *Difficult Labour*, gives a fairly detailed description with several illustrations, taken from Ribémont-Dessaignes and Lapage. He quotes the opinion of Mme La Chapelle and Matthews Duncan that it is more common, even when a central rupture has taken place, for the child to emerge through the proper orifice.

Zangemeister (1927) in his *Lehrbuch*

der Geburtshülfe gives the incidence of central rupture of the perineum as 0.03 per cent, or 1 in 3,000 labours.

Munro Kerr (1937) refers briefly to the condition, but states that in many cases the rectum is involved in the tear. It seems from the reports of the literature that this complication is rather unusual, and that the rectum and anal canal often escape.

He also describes a case where a primipara was brought to the hospital with the foot of the child protruding through the anus, although no attempt had been made to deliver the child.

Stoeckel (1938) in his *Lehrbuch der Geburtshülfe*, describes the following as aetiological factors in the production of central rupture of the perineum: high perineum, steep pelvic angle, narrow and rigid introitus, especially from old tears, friability of the posterior vaginal wall and the adoption of the squatting position. He notes that a hand or foot of the child may emerge first even with a vertex presentation.

CONCLUSIONS.

The mechanism by which the child and placenta escaped through a rent in the posterior vaginal wall and perineum seems to be fairly easily explained in the case which has been described. Little is known about the patient's first confinement, but she was confined in her own home, was told that she had had an internal tear, and sutures were inserted by a midwife. It seems likely that these sutures were inserted through the skin only and that scarring resulted in the perineal area with a weakness in the lower part of the posterior vaginal wall. In the 2nd labour, delivery could be described as precipitate. As the head came down on to the perineal body, the rigidity of the previously sutured area prevented the usual distention of the vulval orifice. The weak area in the posterior

vaginal wall gave way, and the child's head came to lie in the fascial space posterior and lateral to the vagina. The force of the uterine contractions then drove the head through the skin of the perineum and that overlying the left labium majus. The child emerged very much to the left side, and it is possible that a congenital hernia or weakness of the pelvic floor, as described by Kovacs (1942), was present in this case.

Radiological examination of the pelvis did not reveal any evidence of contraction of inlet or outlet nor any abnormal configuration of the sacrum. Pelvic contraction does not seem to have been a predisposing factor in this case.

Obviously this patient should have had an episiotomy as soon as the true state of affairs was revealed. It is unfortunate that delivery was so rapid that skilled aid could not be obtained in time for this to be performed, as it is probable that the very extensive laceration of the vaginal wall would have been prevented by this means.

It is of further interest to note that local analgesia, combined with premedication, was entirely satisfactory for the repair of this extensive laceration.

SUMMARY.

A case is presented where spontaneous delivery took place through the perineum, after extensive tearing of the posterior and lateral vaginal walls. The patient had had a perineal tear in a previous confinement. The bony pelvis was normal in size. The literature on central rupture of the perineum is reviewed. It is concluded that when such laceration is threatened, episiotomy should be performed without delay.

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Rupture of the Rectus Abdominis Muscle during Pregnancy

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The relative rarity of this complication of pregnancy and labour is stressed by Thomas,[1] and Torpin,[2] in recently published case reports, indicating that only 32 recorded cases appear in the literature. This communication, therefore, seeks to place on record the clinical and pathological details of another instance of this complication which occurred at the Brisbane Womens's Hospital in June 1939, and to call attention to a report of a similar case which was omitted by Torpin in his otherwise comprehensive review of the literature.

The high maternal mortality (13 per cent) resulting from this condition as a complication of pregnancy[2] is a reminder of the need for early and correct diagnosis, for it is probable that this figure would have been very different if early haemostasis had been effected and modern transfusion facilities used. In only 9 of the 32 cases reported was the correct diagnosis made prior to operation. It is probable that this was due to failure to consider the possibility of such a lesion rather than to difficulty in eliciting the more characteristic physical signs. Careful examination of any atypical features presenting in a case of concealed accidental haemorrhage may possibly lead to a correct diagnosis of haematoma of the rectus abdominal muscle. Personal experience suggests that the condition may be simulated by acute necrobiosis of a uterine myoma, axial torsion of the pregnant uterus,[3] haemorrhage into an ovarian cyst with twisting of its pedicle, and acute hydronephrosis.

Case Record.

Mrs. F.W., aged 36 years, was pregnant for the third time. Her previous obstetrical history did not contain any significant features; both infants had been born at term and there had not been any miscarriages. (Physical examination subsequently revealed a systolic and diastolic murmur at both aortic and pulmonary areas; the blood Wasserman reaction was negative.)

At the time of admission to the Brisbane Women's Hospital at 10.45 p.m. on June 24th, 1939, her pregnancy had advanced to the 34th week. It was learned that the patient had had a troublesome cough for several weeks and that during the previous 24 hours it had been associated with distinct pain over the right side of the abdomen whenever a bout of coughing occurred. Three hours prior to admission she had been seized with persistent pain in this region, which had now become very tender. She had felt faint and expressed the opinion that the abdomen was swollen on that side.

On examination the patient was pale and somewhat distressed. The pulse-rate was 120 and the temperature, although normal on admission, registered 97.8°F. a few hours later. Her urine was free of albumin and the blood-pressure was 125/70 mm. Hg. The uterus was enlarged to the size of a 34 weeks' pregnancy, and external ballottment of the foetal head could be demonstrated without difficulty above the pelvic brim. The right side of the abdomen, however, from the costal margin to the iliac fossa was the site of a tender, moderately firm, elongated tumour. Palpation of the uterus through the left rectus

muscle showed it to be of normal consistency. Peri-umbilical staining with haemaglobin was absent. The abnormal maternal heart sounds referred to were noted; there were numerous rhonchi on auscultation of the chest. Erythrocytes numbered 2,780,000 per c.cm., and the haemoglobin content was estimated as 50 per cent.

A diagnosis was made of haematoma within the right rectus sheath following partial rupture of the right rectus muscle. Morphine and atropine were administered and codeine in a linctus was given at regular intervals in an endeavour to control the coughing attacks, and a firm abdominal binder was applied. Whilst a compatible blood donor was being sought a period of expectant treatment was followed. On the following morning the clinical picture was not very different from that presented on admission. By 2 p.m., however, the area of swelling and tenderness had extended to the right flank and the degree of tenderness had increased. Subsequently the pulse-rate rose to 168 and the blood-pressure fell to 100/55 mm. Hg.

Further conservative treatment was therefore abandoned and under nitrous oxide, oxygen and ether anaesthesia the right rectus sheath was opened by a paramedian incision approximately 8 inches long. Extensive laceration of the fibres of the right rectus muscle had occurred just below the level of the umbilicus. Almost half the width of the muscle belly on its medial side was involved, but no definite line of rupture could be demonstrated. Blood was still oozing from the ragged muscle edges and spurting feebly from 2 branches of the inferior (deep) epigastric artery; these were secured.

An extensive haematoma consisting chiefly of recent blood clot had formed between the muscle and its posterior sheath superiorly and immediately anterior to the peritoneum and fascia transversalis, inferiorly. Virtually the whole muscle belly had been displaced forward by this huge clot which extended upwards to the right costal margin, down to within 2 inches of the symphysis pubis, and laterally well out towards the flank. The amount of blood clot removed was sufficient to fill 4 standard size kidney dishes.

The space created by the haematoma posterior to the medial half of the rectus muscle was packed with gauze, which was then lead through a wide-bore rubber tube placed in the lower end of the wound. It was anticipated that a pad incorporated in a firmly applied wound dressing would help to obliterate the more lateral portions of the haematoma cavity. The peritoneal cavity was not opened and the incision was closed, using an "anchor dressing" in conjunction with the tension sutures. Replacement therapy using saline by the intravenous route was commenced and this was followed by a transfusion of Group O blood. The pulse-rate was 140 per minute and the general condition of the patient was fair when she left the theatre. Oxygen was administered by an intranasal catheter and nursing was carried out with the patient in a semi-sitting position as soon as she had recovered from the anaesthetic. The administration of sulphapyridine in full dosage was commenced and an expectorant mixture was given in place of the linctus.

On June 26th, however, the patient was still very ill; her temperature had risen to 100.6°F. and the pulse-rate varied from 130 to 140 per minute. Some upper abdominal distension was present. Auscultation of the chest revealed abundant moist sounds. Subsequently signs of peripheral circulatory failure developed with a rapid, irregular pulse, falling blood-pressure and intense pallor. The patient died during the day.

Autopsy was performed and it was then learned that in addition to the findings made at operation, the haematoma had infiltrated into the right parametrium, separating the layers of the broad ligament. Early pneumonic consolidation was present in the upper lobe of the left lung and both lower lobes were intensely congested. No abnormal changes had occurred within the uterus (Caesarean section had been performed immediately after the death of the mother, but the infant was stillborn).

DISCUSSION.

Quite the best account of the condition of haematoma of the rectus abdominis muscle comes from the pen of Cullen and Brödel.[1] The causes are listed as muscular exertion, pregnancy, typhoid fever, influenza or influenzal pneumonia, heart disease, haemorrhagic diathesis, gall bladder disease, tetanus, syphillis and occasionally, by direct violence. When

seen in association with typhoid fever and influenza, extensive waxy degeneration of the rectus muscle, "Zenker's degeneration," has been observed. In such cases the muscle is brittle and easily torn. When haematoma of the rectus muscle has developed as a complication of pregnancy however, a history of trauma or abnormal muscular stress appears to be more common that a record of previous debilitating or constitutional disease. Thus in Torpin's series only 1 case was associated with typhoid fever, and 2 with influenza, whilst 15 cases had a cough of varying severity and duration, 5 developed the haematoma during the course of labour and in 2 cases the lesion followed a fall. The same type of observation is made in the more recently reported cases, 1, 5.

But however significant these factors may appear as a precipitating cause in the production of the haematoma, the frequency of cough as a symptom during otherwise uneventful pregnancies, and the rarity of rectus injury as a complication of labour, suggest the presence of some, as yet unknown, predisposing factor of aetiological importance. Whilst evidence of previous debilitating disease is rare, multiparity is the rule and the complication is essentially one of late pregnancy when the recti are stretched over the enlarging uterus.

Yet unless we are to believe that rupture of the rectus abdominis in multiparae approaching term or in labour is a purely accidental and fortuitous occurrence (as, of course, it may be), these observations have no real significance of an aetiological nature. Is there any further line of approach in the search for more specific predisposing factors? Bourne[6] has recently expressed the thought that must have been in the minds of many obstetricians in reference to the varying effects of pregnancy on the subsequent structure and tonus of the anterior abdominal wall. He states: " a first pregnancy may be followed by a long, perhaps permanent, period in which the abdominal wall is slack and toneless, whilst on the other hand some women who have had many children manage to preserve a good abdominal contour. There is some factor, deeply inherent in the individual, which influences muscle tone and which confers on him or her their characteristic type. This has nothing to do with muscular development or strength." Bourne suggested that an endocrinal factor was probably involved.

It may be that the same factors that determine which patient shall suffer permanent damage to the abdominal recti (in the absence of hydramnion or twin pregnancy) are also operative, though of course to a greater extent, in predisposing certain multiparae to the formation of haematoma in the presence of a precipitating cause. Several authors have put forward the suggestion, which in some instances has been confirmed, that the development of small haematomas within the rectus sheath during pregnancy is not an uncommon occurrence. Thus Hobb's case,[7] a 6-para who suffered a fatal haemorrhage into the rectus sheath during the 39th week of her pregnancy was found at autopsy to have a sausage shaped tumour distending the left rectus sheath from the pubes to the costal margin. There was a large ragged tear on the posterior surface of the muscle belly at the junction of its middle and lower thirds, and 3 pints of blood clot were removed. There was evidence of previous small tears with old blood clot attached in the upper portion of the muscle. Torpin expresses the opinion that an appreciable number of haematomas of the rectus muscle in pregnancy and labour are small, undiagnosed and consequently unreported.

From the point of view of diagnosis Cullen states that haematoma of the rectus muscle has simulated nearly every form of acute abdominal lesion. In addition to the conditions already referred to in this paper he suggests the possibility of confusion with abdominal hernia, acute appendicitis, thickening of the sigmoid colon and gall bladder disease. Staining of the peri-umbilical abdominal fat is likely to be present only when rupture of the rectus sheath has occurred. In the more obscure cases incision of the rectus sheath is necessary before the true nature of the condition can be recognized.

Dixon Hughes'[8] case, which was the 1 omitted from Torpin's series, is chiefly of interest from the point of view of diagnosis. The patient was an 8-para in the 38th week of her pregnancy. Again a severe cough was prominent in the history. The possibilities considered had been degeneration in a myoma, accidental haemorrhage, twisted ovarian cyst and hydronephrosis. A urogram revealed a large renal calculus and a hydronephrosis. The latter was drained by ureteric catheterization, but the tumour remained. Subsequently a para-rectal incision was made and an amount of blood clot sufficient to fill a large kidney dish was removed from behind the right rectus muscle. A branch of the inferior epigastric artery was secured. The patient did well.

Consideration of the anatomical aspects of rupture of the rectus abdominis reveals several points of interest. Although the lesion may occur in any part of the muscle it is usually found below the level of the umbilicus where, for the greater part, the posterior sheath is missing, so that the blood lies between the muscle and the peritoneum. It is because of the peritoneal irritation resulting from a haematoma in this site that symptoms simulating various acute abdominal conditions have been described.

Actual rupture into the general peritoneal cavity is most uncommon and the surgical treatment of haematoma of the rectus sheath should not entail opening into this cavity.

The reason for the higher incidence of these lesions within the lower half of the rectus sheath is not immediately obvious. Walmsley,[9] writing on the anatomy of the anterior abdominal wall, points out that the recti (and in man the external obliques), through their attachment to the thorax above and the pelvis below, are concerned in the maintenance of posture and anteroposterior movements of the trunk. The hypogastric region, however, since it lies between the iliac bones, and is in this sense part of the pelvis and moving with it, does not take part in these movements. It is in this "skeletal" area that the rectus is unsegmented and largely unattached to the sheath except along the linea alba.

I would suggest that in the unsegmented and unattached condition of the rectus muscle in the hypogastrium may lie the explanation of the greater incidence of rupture within this area. Ligget's[10] case is worthy of mention because of the atypical site of rupture. The fibres of the right rectus muscle had been torn opposite the tip of the 9th costal cartilege with the production of a localized tender swelling in the right hypochondrium, but no symptoms suggestive of an abdominal emergency. The patient, who was 7 months pregnant at the time of the incident, continued to term after the clot had been evacuated and was subsequently delivered *per vaginam*.

Reviewing briefly the matter of treatment, it is now evident that an expectant policy is rarely the correct one. Because of the anatomical considerations obtaining, there is little to prevent a subumbilical haematoma from extravasating widely with peritoneal irritation and shock aggravating the symptoms arising from the haemorrhage itself. On the other hand, a

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small well-localized tumour in the upper portion of the rectus, though correctly diagnosed as a haematoma, may well be treated conservatively in the absence of any increase in size.

SUMMARY AND CONCLUSIONS.

1. A fatal case of rupture of the rectus abdominis muscle, occurring during the 34th week of pregnancy, is recorded.

2. Aetiological factors in the production of this type of lesion, as a complication of pregnancy and labour, are discussed.

3. The literature on the subject is reviewed with special reference to diagnosis, anatomical considerations, and treatment.

4. Suggestions in regard to aetiology and conclusions in respect of treatment are offered.

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An Uncommon Sequel of Secondary Rupture of the Uterus

BY

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DANGER of secondary rupture of the uterus led to the dictum "once a Caesarean section, always a Caesarean". Secondary rupture may be so unobtrusive as to merit the designation "silent". Silent rupture may give great difficulty in diagnosis.

According to Berkeley *et al.*,[1] some secondary ruptures occur in pregnancy, but most occur early in labour. Some occur before the onset of labour, even forestalling obstetric presentiment,[2] others—the more predictable—occur during the course of labour, or in the process of extracting an aftercoming head, or in removal of an adherent placenta.

Silent rupture occurred in the case now reported, and the sequel of this rupture is worthy of record.

Mrs. C. R., aged 36, 6-gravida.

Previous obstetric history. The first 3 were normal pregnancies with spontaneous deliveries. The 4th pregnancy was terminated 3 days before term by classical Caesarean section for central placenta praevia on April 4th, 1940. The 5th pregnancy reached term and a 3-hour labour ended on May 5th, 1943, in spontaneous delivery of a 7¾ pounds baby.

Present pregnancy. The patient had arranged to have her confinement in her own home, and the expected date of delivery was January 17th. All was well until January 16th, when the patient experienced tumultuous foetal movements. Thereafter no sign of life was felt. She was seen at home by her medical attendant who apparently heard foetal heart sounds and assured her that the foetus was still alive. A period of 7 weeks elapsed and the patient still did not go into labour. Two days of slight haemorrhage then occurred and on

suspicion of recurrent placenta praevia the woman was sent to hospital.

On admission her general condition was good and the slight bleeding stopped in 24 hours. The abdomen was free from tenderness. There was some excess of liquor and the foetus was mobile from transverse to breech. Foetal heart sounds could not be auscultated. Examination of the blood showed a negative Wassermann reaction, and blood grouping showed Group A, Rhesus positive (subgroup Rh_1). The husband also belonged to Group A, and to the identical Rhesus subgroup. X-ray of the pregnancy revealed Spalding's sign which confirmed clinical suspicion of foetal death.

Treatment. The risk of secondary rupture seemed worth taking in view of the intrauterine death. Accordingly the lie of the foetus was made longitudinal by external version and the membranes ruptured by the use of a Drew Smythe catheter. Meconium blocked the catheter when a pint of liquor had been withdrawn and the catheter was removed. Oral Stilboestrol, and intramuscular oestrogen were given to sensitize the uterus.

Progress. The patient remained without pain of any kind for 18 days. Five days after induction the temperature and pulse-rate became elevated and simultaneously the meconium-stained liquor which had been trickling gave place to free loss of offensive discharge. A full course of sulphathiazamide was prescribed and low-pressure vaginal irrigations given at 4-hour intervals. The 6th and 7th days were less febrile, but on the 8th intramuscular penicillin injections at 3-hour intervals were given as there was recurrence of febrile disturbance. The cervix was examined at this time and found to be 1 cm. dilated. Penicillin therapy was continued during the 9th, 10th, 11th and 12th days. By the 13th day the general condition had somewhat improved and under intravenous anaesthesia the cervix was dilated with difficulty to 2½ cm. and

a leg was brought down. A fillet was attached to the leg and a 2-pound weight applied. The general condition improved during the 14th to 17th days, but pains did not occur and advance of the leg was not observed. On the 15th and 17th days a pint of blood was transfused.

Delivery. On the 18th day some advance of the leg was noticed although there was still no pains. With slight additional traction and pressure on the fundus, the putrid foetus escaped *per vaginam*. The birth was followed by a despumation in which the placenta and 3 pints of foul blood-stained greenish fluid escaped. Ergometrine was given intramuscularly, but there was no postpartum haemorrhage. On the following day a 3rd pint of blood was transfused.

Puerperium. On the 5th day following delivery, the temperature rose again to 104°F. and the patient complained of pain and tenderness in the right epigastrium. On palpation of this region a mass was felt with hard sharp edges just below the skin. With gentle pressure crepitus was elicited. Radiography revealed the mass to contain bones derived from the foetal skull (Fig. 1). A period of 4 days was allowed for further penicillin treatment and for localization of sepsis in the abdomen. On the 9th day of the puerperium, the mass was more superficial and sequestrectomy was undertaken. This was effected under local infiltration anaesthesia supplemented by inhalation anaesthesia during actual removal of the bones.

Operation Notes. A 3½-inch upper right rectus incision was used. The rectus was split over the apex of the mass. The peritoneum was found to be congested and when incised grey-green pus escaped. The abscess had two loculi, one antero-posterior and the other transverse. The line of the incision was common to the planes of both loculi which were disposed at a right angle. From the anteroposterior loculus one frontal bone and one parietal bone were removed, and from the transverse came the other frontal bone. Thereafter a free escape of greenish pus occurred. A rubber drain was inserted to the depth of each loculus and the abdomen closed. Penicillin was instilled through the drainage tubes into the abscess cavity twice daily for 4 days, after which the tubes were removed. The patient made a rapid recovery and was ready for discharge to a convalescent hospital

11 days later. Three weeks later she was allowed home, on condition that she reported for follow-up.

In order to determine the extent of healing of the rent in the uterus, a hysterosalpingogram was made 8 weeks after confinement (Fig. 2). Rotary displacement of the uterus was noted but there was no " spill " through a uterine fistula as might have been expected.

Twelve weeks after confinement there has still been no menstruation, nor has there been abdominal discomfort suggestive of menstruation into the abdomen. The patient is very well, the abscess scar is sound, but there is still a minute discharging sinus in the wound. She has wisely consented to have menstruation stopped by X-ray therapy.

DISCUSSION.

A case of silent secondary rupture of the uterus is recorded. When first seen in hospital the pregnancy had exceeded by 8 weeks the time for repeat elective section,[3] and intrauterine death had taken place. Delivery was eventually effected 10 weeks after term.

In view of the intrauterine death it was decided to incur the risk of secondary rupture, about 2 per cent according to Delfs and Eastman,[4] by attempting vaginal delivery. Unfortunately, rupture took place and was of the silent variety. As in 25 per cent of such cases,[4] shock and pain were absent. Tenderness over the uterus may have been present but it was discounted as due to putrefaction. True labour pains did not occur, indeed at one stage it appeared that it would become necessary to dilate the cervix and perform embryotomy.

From the localization of the bones as found at sequestrectomy, it is presumed that the bones passed through the rent together. Their escape was aided by their serrated edges, by the presence of putrefaction, and by painless detumescence of the uterus. It is a matter of conjecture whether the bones passed through the uterus

FIG 1.
Radiograph showing sequestra in abdomen

FIG 2
Hysterosalpingogram eight weeks after delivery.

F.F.

before the leg was secured *per vaginam*, during the spell of traction on the leg, during delivery of the aftercoming head, or in the early puerperium. It seems possible that the "artificial" delivery *per vaginam* may have arrested a "natural" expulsion of the foetus into the abdomen, but more probable that the bones were left in the uterus after delivery and their escape aided by the prophylactic administration of ergometrine. Migration of foetal parts towards the surface of the abdomen is not uncommon in secondary abdominal pregnancy,[5] and could presumably obtain in this instance.

Conservative treatment has been advocated by Herbert Spencer,[6] Munro Kerr,[7] Naguib Mahfouz Bey,[8] and others in the treatment of rupture of the uterus. The mortality with conservative measures is surprisingly low.[7] It came to be applied indirectly in the case recorded and the result has been excellent considering the gravity of the sequel.

If the gravid uterus containing the dead foetus had been left alone it is possible that uterine rupture would still have supervened and been followed by formation of a lithopaedion.

CONCLUSION.

Recovery of foetal parts from the abdomen has been reported in extrauterine pregnancy. The case recorded illustrates this as a possible sequel of silent rupture of the uterus.

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The Effect of Oestrogen (Stilboestrol) on the Formed Elements of the Blood in Women*

BY

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LARGE doses of oestrogens exert a profound influence upon the blood picture of some species of animals. Arnold and co-workers (1936, 1937) found that large doses of oestrogen suppressed haemopoietic processes to such an extent that death resulted. Balo and Purjesz (1937), Bareuther and Schabbel (1937), Tyslowitz (1938) reported gradual anaemia, haemorrhagic purpura and leucocytosis followed by a leucopenia in dogs after the administration of natural oestrogens. Tyslowitz (1939), Arnold (1939), and MacBryde *et al* (1940) repeated the above experiments using diethylstilboestrol (stilboestrol) and obtained similar results.

Crafts (1941) repeated the experiments with natural and synthetic oestrogens in dogs and monkeys and found in the dog that stilboestrol caused a marked neutrophilia followed by a decrease in the young neutrophils, anaemia, and a decrease in haemoglobin. Daily doses of 5 mg. of alpha- or beta-oestradiol produced similar results. In monkeys Craft reported that 10 mg. doses of stilboestrol did not produce the condition found in dogs but there was a slight anaemia. Even fourfold dosage of stilboestrol per kg. of body weight in the monkey did not produce the blood picture found in dogs with 5 mg. daily doses of the same oestrogen.

Tyslowitz (1941) studied the blood picture in some of the monkeys in the Carnegie colony in Baltimore and stated that "the blood picture suffered little change" when these animals were treated with large doses of oestrogens.

Shute (1946a) states that women who have prolonged bleeding and coagulation time usually have high blood oestrogen levels and that vitamin E corrected this. He also quotes Castrodale and his associates and Tyslowitz and his co-workers that the administration of oestrogens to dogs decreases the blood platelets even to purpuric levels. Shute (1946b) concluded that stilboestrol would lower the platelet count and cause purpura in women receiving stilboestrol, so it was thought a study of some of the formed elements of the blood in women should be reported because stilboestrol is being used more and more.

Methods.

One hundred and sixty-three pregnant and non-pregnant women coming to the Out-patient Menstrual Disorder Clinic, Jefferson Davis Hospital, were given various dosages of stilboestrol by mouth and intramuscularly for various periods of time from 1 week to 1 year. In some the dose was increased every 2 to 6 weeks.

In some patients stilboestrol was stopped for 4 weeks to 6 months and then started again.

Blood platelet, red-blood cell and white-blood cell counts and haemoglobin deter-

minations were made before, during and after stilboestrol was given.

RESULTS.

In 93 platelet counts before stilboestrol medication the average was 268,124.

In 639 platelet counts during stilboestrol medication the average was 261,756. These patients had daily stilboestrol dosages from 0.125 to 2,000 mg.

In 168 platelet counts after stilboestrol medication the average count was 267,380. These patients had total stilboestrol dosages from 0.7 to 111,000 mg.

In 211 red-blood counts before stilboestrol medication the average was 3,677,109.

In 861 red-blood counts during stilboestrol medication the average was 3,578,850.

In 229 red-blood counts after stilboestrol medication the average was 3,616,900.

In 209 white-blood counts before stilboestrol medication the average was 6,213.

In 689 white-blood counts during stilboestrol medication the average was 7,058.

In 194 white-blood counts after stilboestrol medication the average was 6,851. These patients had total dosages of stilboestrol from 0.7 to 111,000 mg.

In 201 haemoglobin determinations before stilboestrol medication the average was 71.8 per cent.

In 688 haemoglobin determinations during stilboestrol medication the average was 74.6 per cent. These patients had daily dosages of stilboestrol from 0.125 to 2,000 mg.

In 192 haemoglobins after stilboestrol medication the average was 76.9. These patients had total dosages of stilboestrol from 0.7 to 111,000 mg.

Table I shows the number of mg. of stilboestrol taken and the number of patients receiving those amounts.

TABLE I.

No. of patients	Total No. of mg. of stilboestrol
26	0.7 to 25
20	26 to 50
11	51 to 100
10	101 to 150
4	151 to 200
4	201 to 250
1	251 to 300
2	301 to 350
2	351 to 400
2	401 to 450
3	451 to 500
3	501 to 550
4	551 to 600
1	601 to 650
1	650 to 700
3	701 to 1000
7	1001 to 2000
4	2001 to 3000
5	3001 to 4000
5	4001 to 5000
3	5001 to 6000
4	6001 to 7000
5	7001 to 8000
2	8001 to 9000
4	9001 to 10,000
10	10,001 to 15,000
3	15,001 to 20,000
3	20,001 to 25,000
2	25,001 to 30,000
4	30,001 to 40,000
2	40,001 to 50,000
1	50,001 to 60,000
1	60,001 to 70,000
1	70,001 to 111,000
163	

DISCUSSION.

In dogs large doses of stilboestrol caused marked changes in the blood picture while in monkeys there was little, if any, change.

In our series in women the blood picture was not altered from the control before and after stilboestrol, even when a total dosage

of 111,000 mg. of stilboestrol was given over a period of 1 year.

We might fairly conclude that stilboestrol produces no changes in the haemopoietic process in women. The platelet count was approximately the same before, during and after stilboestrol.

No patients developed purpura haemorrhagica, nor did the abdominal or perineal incisions bleed more in those undergoing operation.

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The Familial Incidence of Adrenal Hypertrophy and Female Pseudohermaphroditism

BY

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THE cases described in this paper are those of 2 female pseudohermaphrodite infants occurring in the same family. At the death of the first the mother was advised to have a further pregnancy because it was considered unlikely that this malformation would recur. When it was exactly reproduced in the subsequent child it was thought of value to determine how frequently this defect is familial.

Two types of pseudohermaphroditism should be distinguished. The male pseudohermaphrodite is of male genetic constitution, but factors operating during development modify growth in the female direction. There is therefore hypospadias of varying severity, often maldescent of the testes and effeminate bodily form. There is rarely any anatomical abnormality of the endocrine glands. Male pseudohermaphroditism is well recognized to be inherited and Witschi (1939), reviewing the literature, records 11 families with a total of 42 male pseudohermaphrodite individuals.

In the female pseudohermaphrodite the genetic constitution is female but hormonal influences during intra-uterine life lead to masculinity. Individuals with this defect show hypertrophy of the clitoris, varying degrees of maldevelopment of the vagina and as growth proceeds a masculine bodily form. The cortex of one, or more commonly both, adrenals is hypertrophied.

Although these 2 types of pseudohermaphroditism are genetically and developmentally quite different the distinction between them may be very difficult, and in many cases impossible, without a laparotomy. It is not uncommon for a pseudohermaphrodite to be brought up as a member of the wrong sex, or for the sex to remain in doubt throughout life.

The present cases are typical examples of female pseudohermaphroditism. The infants were the 2nd and 3rd children of normal parents who were not related to each other. Similar abnormality could not be traced in the family. The 1st child is a normal female, now aged 7 years.

CASE 1. The child weighed 8½ pounds at birth and was considered to be a female because there was some loss of blood from the vulva during the first few days of life. There was marked hypertrophy of the clitoris and no vaginal orifice was seen. During the 3rd and 4th weeks there were feeding difficulties which necessitated treatment at the clinic. At the 4th week severe vomiting and loss of weight commenced and persisted until death at the age of 6 weeks. During the terminal illness a paediatrician noted palpable masses in the loins; these at the time were thought to be enlarged kidneys but in view of the postmortem findings may well have been the hypertrophied adrenals.

CASE 2. The 3rd child was born 2 years later and weighed 9 pounds. There was gross hypertrophy of the clitoris and no vaginal orifice was seen. The determination of sex aroused considerable discussion and on the whole opinion favoured the diagnosis of a male. The baby was well until 4 weeks old, when it died in the course of a day from a sudden attack of vomiting.

Postmortem findings. The postmortem appearances of the 2 infants were similar except that in the first there was considerable wasting and the lungs showed early bronchopneumonia.

Externally there was hypertrophy of the clitoris, which was grooved on its under surface, the groove running backwards to the urethral orifice. The general structure was similar to that of hypospadias in the male. The urethra and vagina had a single orifice externally but the two were separated by a septum which reached almost to the vulva; the urethra and vagina were in fact well developed. Normal uterus and ovaries were present. Apart from the adrenals, the internal organs were not abnormal. The adrenals were enlarged and weighed 8 g. each (normal 3–4 g.). The cortex was finely convoluted, producing a great increase in the total cortical tissue.

Microscopically the clitoris contained much erectile tissue. The rudiments of prostatic glands were present at the base of the bladder, and in the urethro-vaginal septum (fig. 2). The uterus and ovaries were normal (fig. 1). The adrenal cortex was markedly increased in thickness and, compared to the normal, there was less regularity in the general arrangement of the cells. There was no abnormally persisting foetal cortex, but the demarcation between cortex and medulla was less sharply defined than usual (figs. 3 and 4). Fat was almost absent from the cortex. Vines' fuchsinophil reaction for the demonstration of androgens was carried out, but the results were not helpful because there was as much fuchsinophil material in the normal control adrenal. However, the reaction is recognised to be unreliable in postmortem material. The pituitary showed an increase in the proportion of basophil cells in the anterior part. These were all normal granular basophils; none of the hyaline basophil cells described by Crooke were found.

Female pseudohermaphroditism is relatively rare; about 100 cases have now been described. The defect is less clearly hereditary than is male pseudohermaphroditism. However, in a number of families more than one member of a generation were involved. The defect has not been traced through several generations. The abnormality was recorded in sisters by Ogston as early as 1872. Hypertrophy of the

adrenals was specified by Löser and Israels (1923), Polzer and Priesel (1938), and Young (1937) in their cases (Table I). O'Farrell (1935) described a family in which 2 sisters and a cousin were known to be affected, and 2 children who died in infancy probably had a similar defect. The adrenals were not noted, but later a laparotomy on one of these individuals revealed that these were enlarged (Wilkins *et al.*, 1940). Durlacher (1912) recorded cases which might belong to this category but the adrenals were not mentioned. Rhodes (1943) described the abnormality in twins but again the adrenals were not examined. Two other families were recorded by Apert (1928) and Orel (1929), in which the adrenals are said to have been enlarged, but the original papers are not available.

An exactly similar hypertrophy of the adrenals may occur in the male, leading most commonly to enlargement of the penis, hirsutes, rapid growth, unusual muscular development and premature fusion of the epiphyses (Rolleston, 1936; Priesel, 1931; Cohen, 1946; Jacobzimer and Gorfinkel, 1936; Wilkins *et al.*, 1940). Families are recorded in which a male showed precocious development and a female pseudohermaphroditism (Priesel, 1931, Jacobzimer and Gorfinkel, 1936; Wilkins *et al.*, 1940) (see Table II).

More rarely adrenal hypertrophy in the male may lead to male pseudohermaphroditism and one family is recorded in which both male and female pseudohermaphroditism were associated with adrenal hypertrophy (von Werthemann, 1935: 1941).

The Role of Adrenal Hypertrophy.

The evidence that female pseudohermaphroditism is due primarily to an abnormal secretion of hormones is now very convincing. In certain animals, particularly pigs and cattle, the placental circulation of male and female embryos may

be mingled, and the female becomes a freemartin. The administration of androgens to experimental animals during pregnancy leads to the birth of female pseudohermaphrodite offspring. An interesting case in this connexion was recorded by Brentnall (1945). A woman of 26 with an arrhenoblastoma of the ovary developed virilism during pregnancy and was delivered of a typical female pseudohermaphrodite infant. Where the urine of female pseudohermaphrodites has been examined the excretion of androgens has been found to be above the normal level (Talbot *et al.*, 1942; Fraser, 1945).

A feature of some interest is the occasional coexistence of hypertrophy of the adrenal cortex and interstitial celled tumours of the testis (Wilkins *et al.*, 1940; Cohen, 1946). These tumours alone are well recognized as a cause of precocious development. In some cases a similarity between the tumour cells and those of the adrenal cortex has aroused comment. This association may possibly be connected with an anatomical relationship between the primordia of the adrenal cortex and medullary tissue of the gonad which has been recorded particularly in amphibians (Vannini, 1946).

It has often been suggested that the syndromes which occur with congenital hypertrophy and tumours of the adrenal cortex are similar in the pathogenesis. In both there is an abnormal balance of hormone secretion and a tendency to virilism. It should, however, be noted that in carcinoma of the adrenal cortex there is most commonly some degree of muscular atrophy, osteoporosis, obesity and often insulin resistant diabetes while the androgenital syndrome of congenital hypertrophy of the adrenal cortex is usually associated with precocious muscular and skeletal development and diabetes is rare. This distinction may possibly indicate a preponderance of different hormones in the two

conditions (Albright, 1942). In Cushing's syndrome, characteristic of adrenal cortical carcinoma, there may be a relative excess of the hormones involved in the breakdown of tissue proteins to sugar (notably 17 hydroxy- 11 dehydrocorticosterone) while in the androgenital syndrome hormones of the androsterone group may be dominant.

The rare occurrence of male pseudohermaphroditism with congenital hypertrophy of the adrenal cortex (von Werthemann, 1935: 1941) may possibly be due to an excessive secretion of oestrogens by the adrenal cortex. These cases also have their parallel in cases of carcinoma of the adrenal, for although virilism is the commonest sequel, feminism may occasionally occur (Matthias, 1922; Holl, 1930).

Diagnosis and Treatment.

It has already been emphasized that the diagnosis of sex may be very difficult. In Case 1 the sex was correctly determined by the general practitioner because there was loss of blood from the vulva in the first few days of life. This occurrence suggests the presence of a uterus and may prove a useful diagnostic sign. In the first child also palpable masses were present in the loins. It is not known how frequently the hypertrophied adrenals may be palpable but this finding in a pseudohermaphrodite might suggest that the infant was likely to be a female.

Infants with this type of adrenal hypertrophy not infrequently die in early childhood. Of the 38 cases summarized in Tables I and II, 15 died before the age of 6 years, and 9 before 6 months with diarrhoea or vomiting. Dijkhuizen (1943) published a series of 4 cases in which the vomiting was so severe and persistent that a diagnosis of pyloric stenosis was considered. A similar case was also recorded by Skelton (1945). This feature may

TABLE I.   *The Familial Incidence of Female Pseudohermaphroditism.*

Author and date	Sex	Age	Clinical features	Adrenals	Notes
Durlacher, 1912	F.	20 months	Hypertrophy of clitoris	?	Children large for their age.
	F.	6 months	Hypertrophy of clitoris	?	Two other children died in infancy.
Apert, 1928	F.	—	Hypertrophy of clitoris	? +	
	F.	—	Hypertrophy of clitoris	? +	
Löser and Israels, 1923.	F.	21 years	Hypertrophy of the clitoris	Demonstrated to be enlarged by X-ray	
	F.	19 years	No separate vaginal opening		
			Male bodily form		
Orel, 1929	F.		Hypertrophy of clitoris	? +	
	F.		Hypertrophy of clitoris	? +	
Rupilius, 1933	F.	1 month	Hypertrophy of the clitoris and no separate vaginal opening	Enlarged adrenals demonstrated at postmortem	Both children died. Four other normal children.
	F.	4 months			
O'Farrell, 1935	F.	24 years	Hypertrophy of clitoris	Enlarged adrenals seen at operation	Eight normal children.
	F.	19 years	Hypertrophy of clitoris	?	
	F.	9 years	Hypertrophy of clitoris	? \	Three normal children. Cousins of above.
	F.	Dead	Hypertrophy of clitoris	?	Died in infancy.
	F.	Dead	Hypertrophy of clitoris	?	Nine normal children. Cousins of above.
Young, 1937	F.	16 years	Hypertrophy of clitoris Vaginal opening into urethra Male bodily form and hirsutes	Enlarged adrenals demonstrated by X-ray	
	F.	6 years	Similar		
	F.	3 years	Hypertrophy of clitoris Vaginal opening into urethra	+	Children very large for their age.
	F.	8 months	Similar	?	
	F.	16 years	Clitoris 5 cm. long Vaginal opening into urethra	Enlarged adrenals seen at operation	Partial adrenolectomy with doubtful results.
	F	13½ years	Similar		
Polzer and Priesel, 1937	F.	5 months	Hypertrophy of clitoris No separate vaginal opening Prostatic tissue in the urethrovaginal septum	Enlarged adrenals demonstrated at postmortem	Both infants died with diarrhoea and vomiting.
	F.	1 month			
Rhodes, 1943	F.	At birth	Hypertrophy of clitoris	?	Twins.
	F.	At birth		?	
Biggs and Rose, 1947.	F.	6 weeks	Hypertrophy of clitoris	Enlarged adrenals demonstrated at postmortem	Both infants died with vomiting.
	F.	4 weeks	Hypertrophy of clitoris		

FIG. 1 (above). Low power view of the uterus, bladder and part of the vagina in Case 2.

(R.I. P.M. No. 86/46 × 5)

FIG. 2 (below). Higher magnification of several rudimentary prostatic glands taken from the region marked in Fig. 1.
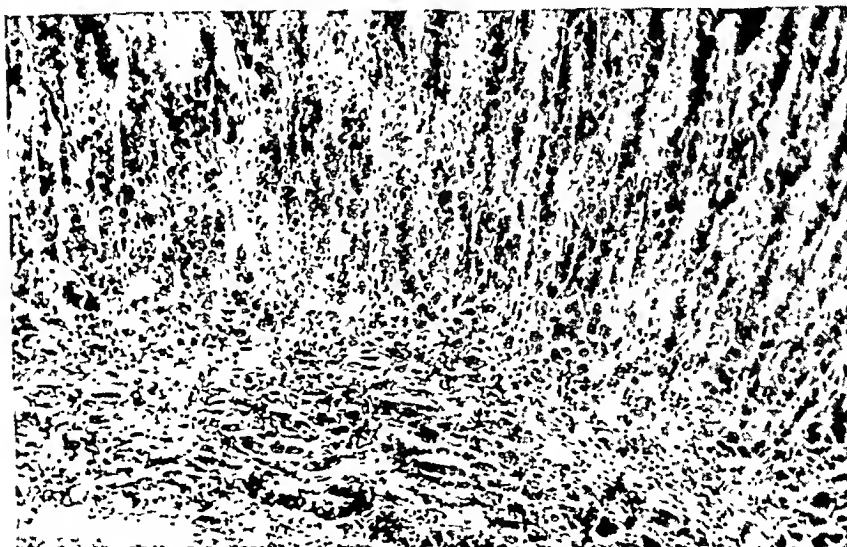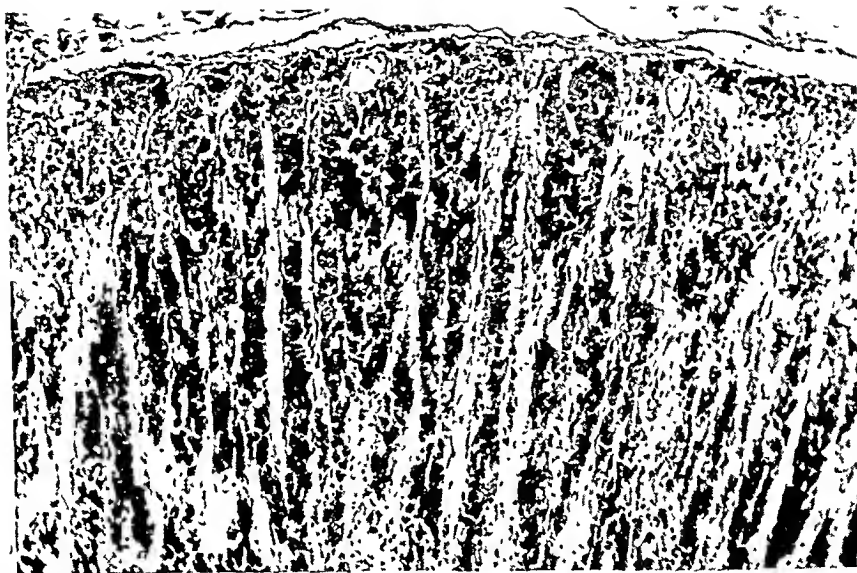
(R.I. P.M. No. 86/46 × 110)

B. & R.

FIG. 3 (above). The outer zone of the adrenal cortex from Case 2.
(R.I. P.M. No. 86/46 × 110)

FIG. 4 (below). The inner zone of the adrenal cortex from Case 2.
(R.I. P.M. No. 86/46 × 110)

B. & R.

possibly be due to desoxycorticosterone deficiency. This suggestion appears reasonable, not only because diarrhoea and vomiting are common symptoms of desoxycorticosterone deficiency, but also in one or two older patients the mode of death was more definitely indicative of adrenal failure. In 1 of these cases described by von Werthemann (1941) the infant had pigmentation of the skin. In the child of 3 years described by Wilkins et al. (1940) death occurred rather suddenly following an indefinite illness associated with pigmentation of the skin, a craving for salt and an elevation of the nonprotein nitrogen to 99 mg. per cent. Then the child of 5 years described by Priesel

of the pneumonia from which he was suffering. The evidence is at least sufficient to warrant the administration of desoxycorticosterone during an attack of diarrhoea and vomiting, or in infections with a disproportionate circulatory collapse.

With regard to plastic operations for the reconstitution of " normal " external genitalia, the only point which requires emphasis is that no such operation should be undertaken without incontrovertible evidence of the true sex.

The question of adrenalectomy in the female pseudohermaphrodite naturally arises. There are two factors which militate against this treatment. In the first place the pathological effects of excessive

TABLE II.

The Familial Association of Female Pseudohermaphroditism with Precocious Development in the Male and Male Pseudohermaphroditism.

Author and date	Sex	Age	Abnormality in sexual development	Adrenals	Notes
iesel, 1931	F.	Infant	Hypertrophy of clitoris	?	Died in infancy.
	M.	5½ years	Precocious development	+	Pigmentation of skin. Died at 5½. Parents related and congenital abnormalities in 2 other children.
cobzimer, orfinkel, 1936	M.	4¾ years	Precocious development	?	Interstitial celled tumour of testis.
	F.	3 years	Hypertrophy of clitoris	?	
	F.	7 months	Hypertrophy of clitoris	?	
ilkins, leischmann nd Howard, 1940	F.	—	Hypertrophy of clitoris	?	
	M.	3 years	Precocious development	+	Died with signs suggesting adrenal failure.
n Werthemann, 935 and 1941.	M.	8 weeks	Atrophic undescended testes—Hypospadias	23 g.	All died in early infancy and postmortems were performed.
	F.	12 weeks	Hypertrophy of clitoris	24 g.	
	M.	8 weeks	Descended testes and Hypospadias	24 g.	
	F. Cousin	4 weeks	Hypertrophy of clitoris	15 g.	Cousin marriage.

(1931) had pigmentation of the skin and died with a very mild attack of scarlet fever. Again, the young man described by Cohen (1946) died with a profound circulatory collapse out of all proportion to the severity

androgen excretion would be far advanced when such an operation could safely be undertaken. In the second place the adrenal hypertrophy is usually bilateral and any partial operation would leave the

original imbalance of hormones. Few cases of congenital adrenal hypertrophy have been subjected to operation and, in comparison with adrenalectomy for tumours, the results are not encouraging.

SUMMARY.

(1) Two cases of female pseudohermaphroditism associated with adrenal hypertrophy and occurring in the same family are described.

(2) The primary defect is probably adrenal hypertrophy, for a similar hypertrophy in the male may be associated with precocious bodily and sexual development.

(3) The defect may be familial in that more than one member of a single generation may be involved. Nine families are recorded in which 2 sisters were pseudohermaphrodites, and in 4 families both males and females were affected.

We should like to express our thanks to Dr. A. H. T. Robb-Smith and Professor Chassar Moir for their interest and assistance. We should also like to thank Dr. Skinner, who first saw these children in general practice and whose interest stimulated this investigation.

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A Fatal Case of Primary Diphtheria of the Cervix and Urethra

BY

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Major R.A.M.C., Gynaecologist,

AND

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Major R.A.M.C., Pathologist.

DIPHTHERIA of the female genital tract is seen sufficiently rarely to warrant the recording of the present case. Few of the standard textbooks contain any reference to the subject, and some of these dismiss it in a few lines as being of extreme rarity (Kerr, *et al.*, 1944; Eden and Lockyer, 1935; DeLee and Greenhill, 1943; Stander, 1945; Wharton, 1943). Beacham and Rice (1944) reported that Eigen in 1932 recorded 115 cases, of which only 72 had been confirmed bacteriologically. They collected 13 more cases from the literature, and added 1 of their own. Primary genital diphtheria is rarely diagnosed, but this may be due to the minimal local symptoms and signs. Parks (1941) pointed out that diphtheritic infection of the vagina and cervix is rare in the adult, as the *Corynebacterium diphtheriae* prefers to grow in air and an alkaline medium.

CASE REPORT.

The patient, an unmarried woman, was admitted to a British military hospital in Germany in May 1946. Two days previously she had started an illness of influenza type, with pyrexia of 104°F. The temperature had fallen to 99°F. the day before admission. Her last menstrual period had started 8 days before admission, and had been normal until the onset of her illness, when the loss became muco-purulent and bloodstained. On examination she was found to be tender in both iliac fossae,

and a diagnosis of salpingitis was made. Nothing abnormal was found on rectal examination. Treatment was instituted with sulphathiazole 20 g. and hot vaginal douches.

She was first seen by one of us (J. B.) on May 14th, 1946. She complained of some breathlessness and pain in the chest. Nothing abnormal was found in the throat, heart or lungs. The menstrual period appeared to be just finishing. The urethral meatus was red and inflamed, and there was a thin urethral discharge. The cervix was red, with some discharge, but there was no membrane. The pelvic organs were otherwise normal. Specimens were taken for bacteriological examination, with the following results:

Smears:

Urethra. Scanty pus cells. Few gram-positive bacilli.

Cervix. Considerable number of pus cells. Scanty gram-positive cocci and gram-positive bacilli.

Cultures:

Urethra. Gram-positive bacilli.

Cervix. Heavy growth of staphylococci (coagulase-positive), and gram-positive bacilli + + + (?Diphtheroid), later identified as *C. diphtheriae mitis*.

Catheter specimen of urine. Moderate cloud of albumen; white blood corpuscles; epithelial cells; and amorphous urates.

Culture: Staphylococci and gram-positive bacilli.

In view of the unusual bacteriological findings further cultures were examined, with these results.

Urethra. Morphological *C. Diphtheriae,* identified as *mitis* strain.

Cervix. *C. diphtheriae* grown, identified as *mitis* strain. Virulence tests were later found to be positive.

Nose and throat. No *C. diphtheriae.*

On the firm diagnosis of diphtheria, treatment was given with intramuscular anti-diphtheritic serum 96,000 units, and an intramuscular drip of penicillin. Polyneuritis and myocarditis were evidently already present when treatment was started, as examination at this stage showed diminished tendon reflexes, associated with tingling in the tongue and limbs. Nothing abnormal was found in the heart and lungs, but the blood-pressure was 85/65. X-ray of the chest was normal. The inflammation of the urethra had cleared up, but there was a profuse, thin, purulent discharge from the cervix and vagina. After treatment, clearance swabs from the cervix were negative, but the patient's general condition deteriorated. The myocarditis progressed. The heart showed multiple extrasystoles, and there was increasing oedema and oliguria. Moist sounds appeared at the base of the right lung. On June 9th the patient had a vagal block attack, and died the following day, after a further collapse which failed to respond to oxygen and restorative measures. Postmortem examination was not performed.

When the diagnosis of diphtheria had been made the patient was questioned as to possible contacts, and she stated that her bethrothed, a " displaced person ", had been in prison 6 weeks previously, and had shared a cell with a man who had diphtheria. We were later able to take swabs from the bethrothed: *C. diphtheriae mitis* was found in the throat swab. *C. diphtheriae* was not found in urethral swabs. The vast majority of cases of diphtheria in Germany at the present time are due to a virulent *mitis* strain of *C. diphtheriae.*)

COMMENT.

The route of infection in a primary case of genital diphtheria is a matter for speculation, but it appears possible that it may sometimes be transmitted by sexual intercourse, although we were unable to establish this in the present case. Opinion is divided on the severity of the condition. Whereas Stander (1945) states that the course is usually benign, DeLee and Greenhill (1943) stress the toxaemic effects in spite of the mildness of the local symptoms and signs, and the present case supports this view. There are sufficient numbers of toxic and fatal cases recorded to indicate that the matter is a serious one (Parks, 1941; Cantrell, 1934; Grant, 1934, 1938). The local signs in the present case were not very marked, and it was impossible to make a diagnosis on clinical evidence alone. In diphtheria, bacteriological diagnosis may be made too late for specific treatment to be effective, as was the case here.

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Haematometra caused by disappearance of the Cervical Canal after Labour

BY

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THE following is a report of a case in which the cervical canal was obliterated after labour, and an account of the conservative surgical treatment of the resulting haematometra.

Obstetrical history. The patient, a primipara, aged 27 years, was delivered on June 9th, 1943. Early in May she showed signs of hydramnios, with a sudden increase in the size of the abdomen in early June. Induction by bougies was carried out on account of acute discomfort and dyspnoea.

The membranes ruptured spontaneously and the os dilated fully but, as there was no advance of the head, forceps were applied, and a stillborn male child was delivered. The placenta was retained and was removed manually. There was a small perineal tear which was repaired.

On June 17th the temperature rose and the patient was transferred to Cheltenham Hospital; she was diagnosed as parametritis and later developed a white leg. Early in August she returned home and was able to resume her household duties.

I first saw the patient on March 27th, 1944. She was complaining of amenorrhoea since her confinement, with attacks of pain at monthly intervals.

Examination. On examination the uterus seemed normal. There was an enlarged left ovary. There was also considerable scarring in the vaginal vault and no cervix could be felt or seen.

Examination under an anaesthetic re-vealed considerable scarring of the vaginal vault, with a small pucker on the right side, which would just admit the point of a fine probe, but this would not enter any distance. The uterus appeared to be slightly enlarged and the left ovary considerably so. I advised the patient that a laparotomy was necessary. She and her husband agreed that this should be done.

Operation. The vagina was packed and the abdomen opened. Fig. I illustrates the condition found. The uterus was slightly enlarged, both Fallopian tubes were distended, the abdominal ends being sealed and the left ovary was obscured by a cystic collection of altered blood. The uterus, at its lower end, was separated from the pack-distended vagina by a flat band of fibrous tissue about an inch in length. The cystic collection of blood was removed from the left ovary, the blood was expressed from both Fallopian tubes, and the uterus opened on its anterior surface. It was full of dark menstrual blood, which was cleaned out. A probe was pushed through the scar tissue closing the lower end of the uterine cavity, and cutting down on this, the uterus was laid open along the whole length of its anterior surface. The vagina was then opened transversely (See Fig. 2). The posterior edge of the vaginal opening was stitched to the uterus so that vaginal mucous membrane was in continuity with the endometrium, the stitching being completed around a tube stitched to the fundus of the uterus and passing into the vagina.
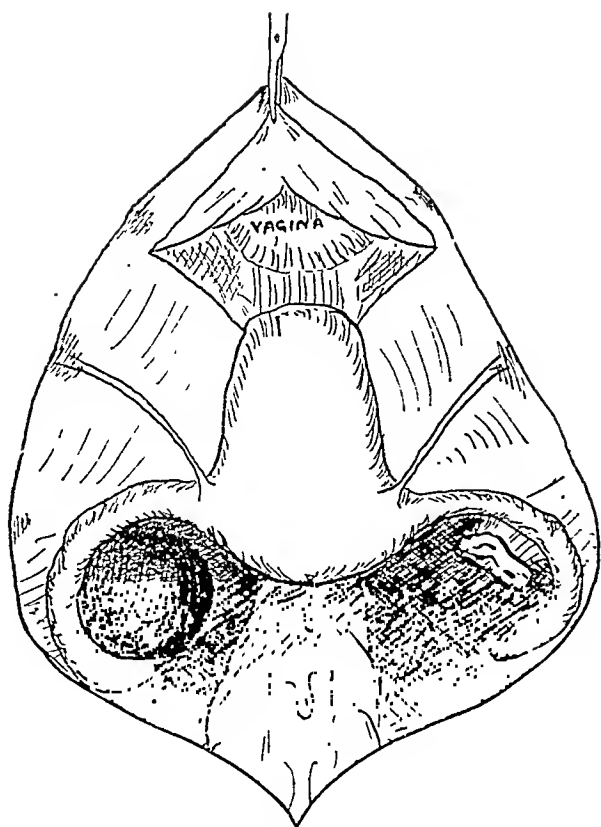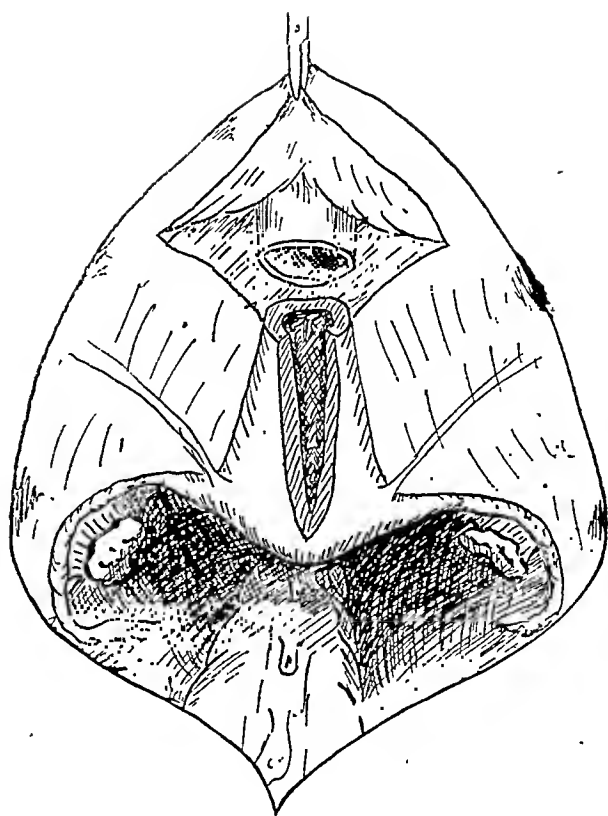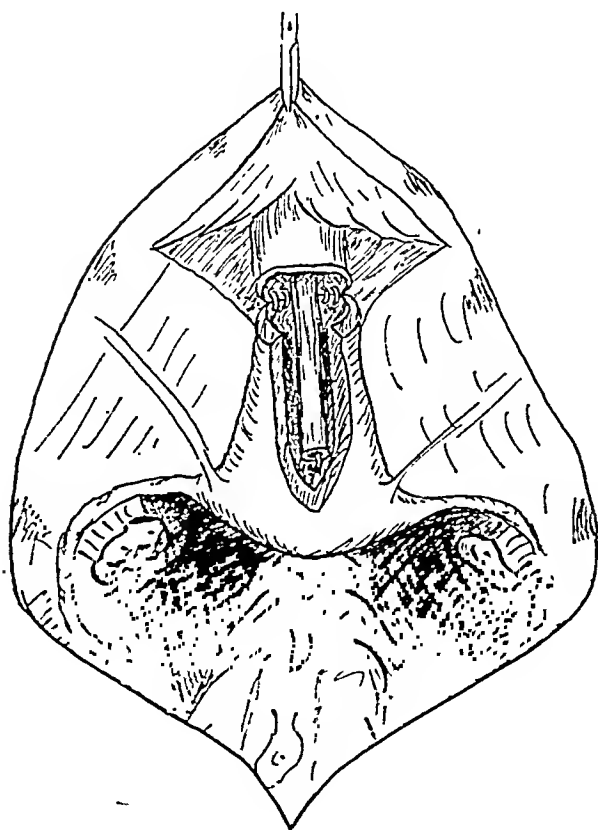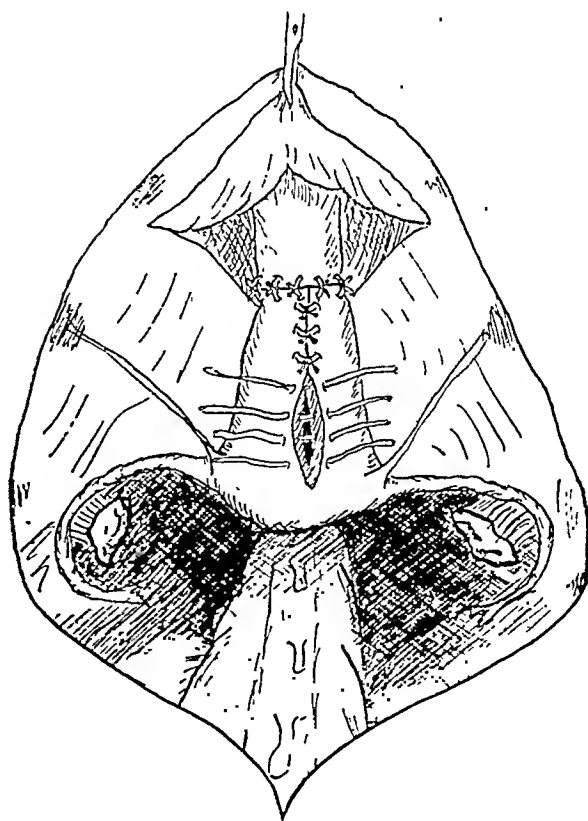
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FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

H.S.A. after V.B.

Repair of the uterus was then completed (Figs. 3 and 4). The tube remained in for 14 days. Convalescence was apyrexial and uneventful. The patient left hospital in under 3 weeks.

The patient was seen again at intervals during the next 5 months. The first period was accompanied by pain on the first day and lasted 5 days. She was examined at the end of the loss. The menstrual flow was coming through a small opening in the scar in the vaginal vault, which would easily admit a probe. She had regular normal 5-day periods with no pain up to the time she was last seen, 5 months after operation, when the pelvic organs were found to be normal on examination, except for the absence of the cervix. She was advised that there was no reason why she should not embark on a pregnancy.

It is doubtful whether, in the absence of a cervical canal, with its ciliated epithelium, a pregnancy will take place, but she has the knowledge that she is still complete and that pregnancy is not impossible.

This case is one of considerable rarity. In a series of 19 cases of haematometra reported by Berstein and Walker (1939) 2 only could be ascribed to obstetric injuries, while Tait (1945) describes a very similar case for which he removed the uterus.

The reason for this record, apart from the rarity of the condition, is to draw attention to the value of a conservative attitude to the surgery of the female generative organs. Hysterectomy is a fatally easy operation, and it is often not realized how mutilating it is, and that the psychological trauma in nearly all women is considerable, and, in the young, very great.

I was fortunate in that I had personal knowledge of a striking case, exemplifying the conservative attitude, in which functioning double uteri were united and joined to an artificial vagina made at the same time by inlay grafting (Bonney and McIndoe).

My thanks are due to Dr. Scott Kerr of Cheltenham for his note of the obstetrical history.

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Foetal Brain Tumour as a Cause of Dystocia

BY

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TUMOUR of the foetal brain as a cause of dystocia is an exceedingly rare condition, and the writer has found only 1 case recorded in the literature which gives a history of difficult labour presumably due to this cause. This case is described by Russell and Ellis (1933), who are more interested in the histological and pathological studies than in the obstetrical significance. They report the case history as follows:—

" Left cerebral glioma in a stillborn infant. Stillborn at term. The mother was 28 years of age. She had 4 children who were alive and well, and no miscarriages. Pregnancy had been normal except for frequency of micturition during the later months. Strong labour pains began on May 24th, 1925. On the following day instruments were unsuccessfully applied by a private doctor. The mother was then admitted to the London Hospital under Dr. Russell Andrews; an anaesthetic was given at 11.45 a.m. on May 26th, 1925, and a 7 pounds stillborn foetus was delivered without instruments. The foetus was in the right occipito-posterior position when the first examination was made and in the right occipito-anterior position when delivered."

A diligent search of the literature has not brought to light report of any case in which a foetus with an intra-cranial neoplasm has survived labour. Such a case might be recorded as one of tumour growth in infancy. In 1,028 records of conditions diagnosed as brain tumours in the National Hospital, London, Critchley (1925) found only 1 case occurring in infancy, the signs developing after birth. In Cushing's series (1927) there were 1,108 verified tumours of the brain, and of these only 24 were in children under 5 years of age. In no case was there reason to suspect the growth at time of birth. He describes a huge teratoma found in an infant 2 months old supposedly normal at birth (Cushing, 1932). The literature dealing with tumours of the brain in infancy has been reviewed by Gross (1934), and in all of the cases recorded the affected infants were apparently normal at birth, the evidence of tumour growth becoming manifest only some time after. In several of these cases, however, signs developed so early as to suggest that the neoplasm was present during intra-uterine life, their sudden appearance, even a few days after birth, being due to the rapid development of hydrocephaly. Hydrocephaly is stated to be the most prominent feature in most cases, and, as obstruction of the cerebrospinal-fluid circulation may be produced by comparatively small tumours, it is possible that if a search were made for the cause in every case of foetal hydrocephaly, the obstructive nature of the lesion would be demonstrated more often than it is. Cushing describes a group of congenital intracranial tumours, the majority representing suprasellar lesions arising from an anlage of Rathke's pouch. While these tumours seriously interfere with development of the pituitary body there is no record of any such tumour showing its presence in the foetus or in early infancy.

The following is the history of a case of

obstructed labour due to a large tumour of the foetal brain.

The patient, a primigravida, aged 25 years, was admitted to the Rankin Maternity Hospital on February 20th, 1943, as a case of prolonged labour. According to the history she was 38 weeks pregnant and had gone into labour on the morning of February 18th, the membranes having ruptured soon after the onset of pains. She was sent into hospital 60 hours later because of failure of the presenting part to advance and because pains had almost ceased. Many vaginal examinations had been made both by the doctor and the midwife, and she had been encouraged to bear down with her pains. On examination she was found to be a well nourished, healthy-looking woman, but quite exhausted. The size of the abdomen suggested a 36 weeks' pregnancy. Foetal heart sounds were present but the position of the foetus was difficult to determine, and the presentation was queried as a breech. Vaginal examination found an oedematous cervix with a 3 fingers' os. The presenting part was high up and difficult to recognize but again breech was queried. It was not impacted but mobile and above the brim. Pelvic capacity was apparently normal. Uterine contractions being absent and the patient exhausted, she was given morphine and scopolamine. She slept overnight and, on the following morning, labour pains having begun again, she was examined under anaesthesia. It was then established that a very large head was presenting but differing from the typical hydrocephalic head in so far that the impression was received of a solid rather than fluid content. Nevertheless it was thought that this was a case of hydrocephaly with the fluid under considerable tension. The skull was then perforated, and, no bone edges being palpable, the case was left to nature. It was noted at the time of perforation that relatively little cerebrospinal fluid escaped and that the skull had not collapsed to the same extent as it usually does in these cases. As labour progressed, however, a very large quantity of tissue was extruded and gradually piled up in the bed. This tissue was whiter in colour and less friable in texture than normal brain tissue, while its mass explained without doubt the enlargement of the head. A sample of this tissue was sent to the pathologist, who reported as follows: —

"The specimen is of brain tissue compressed by a teratomatous growth comprised of mesodermal and ectodermal elements—cartilage and fibrous stroma and glandular elements presenting appearances similar to (1) ovary, (2) alimentary tract, (3) breast or salivary tissue. The stroma varies considerably from 'adult' fibrous tissue to more cellular undifferentiated tissue."

The foetus weighed 4 pounds 13 ounces, and its length was 19 inches. Reconstitution of the head by packing the cranial cavity with cotton wool showed that the occipito-frontal circumference must have been about 19 inches.

Apart from pyelitis which quickly responded to treatment the puerperium was uneventful.

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A Case of Serous Adenofibroma of the Ovary

BY

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AND

A. M. SUTHERLAND, M.D., F.R.F.P.S., M.R.C.O.G.

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SEROUS adenofibroma is one of the rarest of all ovarian tumours. Indeed a careful study of the British literature failed to reveal a single case-report. The subject of serous adenofibroma and cystadenofibroma of the ovary has, however, been discussed in some detail by Scott of Baltimore. He stresses the great infrequency of such cases in the literature, which he sums up as being extremely scant and often questionable because of incomplete descriptions and more recent conceptions of various tumour types. In spite of this, he is of the opinion that they constitute a definite subgroup of serous epithelial tumours of the ovary.

In his review Scott states that in the case reports of ovarian tumours in the files of the Johns Hopkins Hospital, extending over 20 years and embracing a total of 26,000 gynaecological cases, 13 reports of such tumours were discovered and 1 report was found in the general pathology files. Many of these specimens came from other hospitals, some in Baltimore and some in other cities. A number of the tumours, particularly the earlier ones, were filed under other diagnoses.

The clinical features of the 14 cases are summarized and the pathological features are discussed in detail. Scott divides tumours of this type into 2 groups, serous adenofibromas, which are principally solid, and cystadenofibromas, in which some areas are solid and others show large cysts. In his series there were 8 adenofibromas and 8 cystadenofibromas, bilateral tumours being found in 2 patients.

CASE REPORT.

The principal features of the present case are as follows. The patient was aged 56 years and complained of vaginal bleeding of 2 months duration, commencing 11 years after the menopause. She had been married 33 years and had had 2 normal pregnancies. On examination a *large, firm, abdominal tumour was found rising out* of the pelvis to about the level of the umbilicus, a provisional pre-operative diagnosis of fibromyoma being made.

On March 29th, 1946, one of us (A.S) opened the abdomen, when the mass was found to be a solid tumour of the left ovary. The uterus and right Fallopian tube and ovary appeared normal. A small amount of free fluid was present in the peritoneal cavity. Left ovariotomy and resection of a portion of the right ovary were performed, the uterus being conserved. The patient made a satisfactory recovery and was dismissed well on the 22nd day after operation.

The ovarian tumour was firm, compact and lobulated, measuring 7 inches by 5 inches by $4\frac{1}{2}$ inches. On section a few small cystic spaces were seen but the bulk of the tumour was solid. The attached Fallopian tube was elongated but showed no other abnormality. On microscopic examination 2 constituent elements were found, namely a fibromatous stroma and a large number of gland-like or cystic spaces of varying

FIG. I.

s. & s.
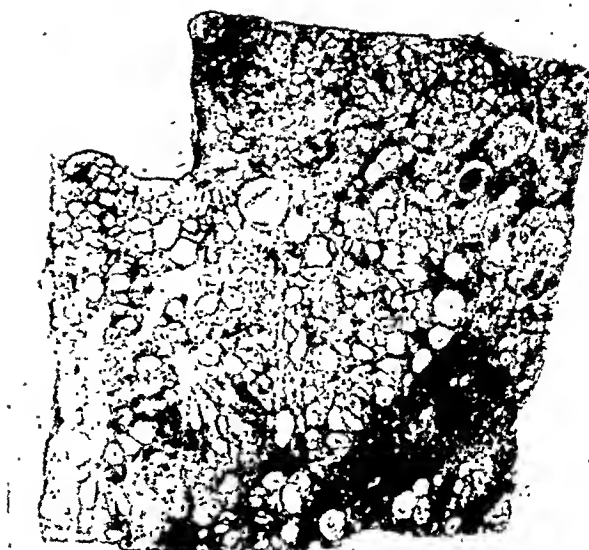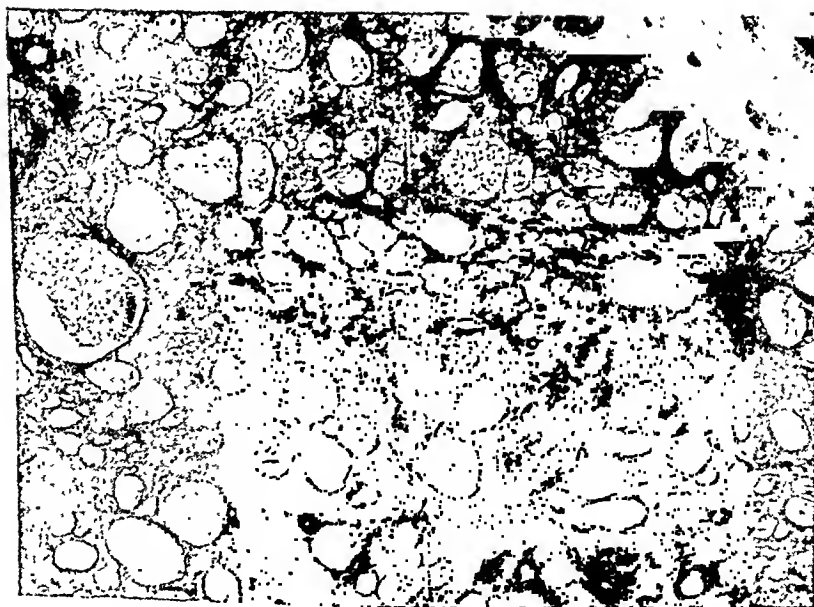
FIG. 2.

FIG. 3.

size. The stroma was exactly the same as that of an ordinary fibroma of the ovary, with narrow strands of fibrous tissue running in all directions. The adenomatous areas were usually circular or oval but occasionally had an elongated or irregular outline. In some places tiny papillary projections into the cyst spaces were seen. The spaces were lined by columnar, cubical or flattened epithelium, which was compactly arranged, usually in a single layer, with centrally-placed nuclei. No evidence of malignancy was found. The histological features are seen in Figs. 1, 2 and 3.

The patient reported 10 months after operation. Since dismissal she had remained well, there being no recurrence of the vaginal bleeding. On vaginal examination the cervix and body of the uterus were found to be atrophic.

Thanks are due to Dr. Emil Novak for his kindness in giving us his opinion on the original sections from this case. Thanks are also due to Dr. Donald McIntyre, into whose wards this patient was admitted.

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ROYAL BELGIAN SOCIETY OF OBSTETRICS AND GYNAECOLOGY

IN accordance with the wishes of the Committee of Management of the former International Congress of Gynaecology and Obstetrics, the Administrative Council and Consultative Committee of the Royal Belgian Society of Gynaecology and Obstetrics, now legal managers of these funds, have decided to utilize the revenues of the Foundation for a prize to the value of 20,000 Belgian francs to be awarded on July 1st, 1949. The prize will be awarded for the best work on Gynaecology and Obstetrics, either in manuscript or published during the 4 years, July 1944 to July 1948.

The works presented should not have already been awarded a prize and should be written in one of the official languages of the International Congress, i.e., English, French, Spanish, Russian, Italian, or German, or translated from one of these languages.

Two copies of the paper should be sent to the Secretary of the Royal Belgian Society of Gynaecology and Obstetrics 12 months before the date fixed for the award of the prize, that is, before July 1st, 1948 (Dr. P. Lavand'homme, 84 av. Paul Deschanel, Brussels).

The examining committee will be chosen by the Royal Belgian Society of Gynaecology and Obstetrics from among its members, honorary members and corresponding members, Belgian or foreign, and according to a method to be ultimately decided by the Society. The president of the Society will be the Chairman of the Committee. Members of the Committee will not be able to take part in the competition.

The decision will be made by a majority vote, and if the Committee decides that none of the submitted works is worthy of the prize, no award will be made and the amount will be added to the value of the next prize.

The prize of the International Foundation of Gynaecology and Obstetrics will be awarded for the second time in July 1949, at the monthly meeting of the Royal Belgian Society of Gynaecology and Obstetrics.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The following candidates have satisfied the examiners for the Diploma in Obstetrics examination.   March 1947.

James Rollo Ballantyne.
Alex Carl Barthels.
Douglas Charles Aitchison Bevis.
Geoffrey Ronald Bourne.
Kathleen Anne Clark Bowen.
John Anthony Bowen-Jones.
Leonard Boyars.
Elizabeth Christian May Brunyate.
Joyce Beryl Burke.
Hubert Cedric Burnell.
John Peter Bush.
Wilfrid Ernest Chapman.
Francis James Cockersole.
Denis Pelles Cocks.
Edward Cope.
George Henry Reginald Curnock.
Alice Davies.
Margret Eley Davies.
James Edwin Drabble.
Patricia Mary Elliott.
Geraldine Winn Everett.
Sebastian Carl Jacques Falkman.
Melville Robert Fell.
Harry Johnson Fisher.
Benjamin John Frankenberg.
Jean Margery Frazer.
George Barton Gibson.
Leslie Stuart Glass.
Cornelius Jeremiah Griffin.
Geoffrey Norman Grose.
Elizabeth Mary Harper.
David Hay.
John Anthony Henderson.
George Sigerson Hopkins.
Jean Anderson Horne.
Brian Gordon Isaacs.
Alun Gareth Jones.
Gordon Davidson Kelly.
Janet Farquhar Kennedy.
Norman Armstrong King.
Donald Victor Latham.
Christopher Lewthwaite.
George Ian Louisson.
Carmichael Mackie.
Archibald Torquil McNeil.

Betty Emma Anna Magill.
David Mander.
Edith Marion Metcalfe.
Reginald Thomas Michael.
Charles Ernest Miller.
Albert Milton.
Doreen Mitchell.
Annapurna Mukherji.
Mathew Robert Neely.
George Frank Newbold.
Dennis Nixon.
Helen Margaret Noble.
Margaret Bonney Noble.
Barbara Dorothy Oakley.
Alfred Denis Parsons.
Stanley Dreland Perchard.
Francis Charles Ralph Picton.
Edward Dennis Pond.
Kenneth Ivor Price.
Sidney Wilson Price.
Margaret Randell.
Edwin Noel Rees.
Rachel Richards.
Leslie Frisby Richards.
Joseph Germain Rountree.
William Sword Russell.
Ruth Sabel.
Timothy John Scannell.
Charlotte Sommer-Hirsch.
Kathleen Heyland Stewart.
Bahman Sohrabji Surti.
Cecil Wallis Sweetnam.
Sheila Royse Tangye.
Mary Elizabeth Tighe.
St. John Michael Alexander Tolhurst.
Eric Frank Twiss.
Michael Joseph Twomey.
William Alexander Walker.
Winifred Isobel Watson.
Constance Margaret Watt.
Cecil Trevor Hamilton Whiteside.
Roberta Williams.
John Kendal Wilson.
Sau Haan Wong.
Elizabeth Younger.

BOOK REVIEWS

"A Textbook of Midwifery." By WILFRED SHAW, M.D., F.R.C.S., F.R.C.O.G. Second edition. J. & A. Churchill, London, 1947. Pp. 649. Price 21s.

THIS textbook is written for the medical student and is likely to appeal to him. It is of suitable size to be carried about and read while he is travelling; yet it is a serious textbook and no mere pocket book. The print is clear, of suitable size and attractive appearance. Illustrations are profuse, of high standard and each makes clear the point which the author wishes his reader to grasp.

The field of obstetrics is adequately covered for a reader who is preparing himself for a qualifying examination in midwifery—especially if used in conjunction with clinical teaching. Fundamentals are presented clearly. The author tries not only to convey factual knowledge, but also to stimulate the reader to think for himself. When, on a particular subject, divergent authoritative views exist the author says so, and endeavours to present fairly to the reader views with which he personally disagrees. He would rather efface himself and his own views than allow his students to become mere sponges, which when squeezed, would give back what they had absorbed. He understands the student mind and so is able to expose and correct many of its misconceptions.

The book opens with an introduction which the student should read as frequently as any other part of the book. It will encourage him to take a broad view of the subject which he is studying in detail.

In a book of high standard it is difficult to pick out portions for special mention. But the haemorrhages, contracted pelvis, abnormalities of uterine action and the pathology of puerperal sepsis read very well.

It is disturbing, however, to find in a book written principally for undergraduates, that forceps delivery before full dilatation of the cervix is not only condoned but even advocated. What Mr. Shaw does himself in this matter is of little consequence. The expert's judgment and skill are such that he can at times afford to defy certain commonly accepted rules. But is it wise to teach this to the unqualified? Will some unfortunate young doctor, having failed with forceps, return home bitterly to re-read these passages to find out how he misinterpreted them? Will quoting Shaw help the hapless candidate who has incurred the examiner's displeasure at the final examination? Is not the newly-qualified doctor better to lose an occasional baby than to subject the mother to the fearful risk of his applying forceps before the cervix is fully dilated?

Recent work on the rhesus factor and erythroblastosis is adequately summarised. The place of penicillin in the treatment of puerperal sepsis is sketchy. It is unusual to find the original red prontosil (sulphonamide crysoidin) preferred to the sulpha drugs now in common use. The advocated technique of swab taking from the cervix for bacteriological diagnosis in puerperal fever is rather elaborate. The busy doctor will not do it. A simpler technique for the taking of a high *vaginal* (rather than cervical) swab would be more acceptable to him, easier to do and less likely to be omitted altogether.

In spite of these criticisms the book should prove popular and can be recommended with confidence.

"Laparotomia Estetica en la Mujer" (Aesthetic Laparotomy). By Dr. CARLOS LORCA. Pp. 66; 70 illustrations. Madrid: Editorial Cientifico Medica, 1946.

THIS gracefully written and produced monograph is dedicated, in the author's words, to the prevention of the mental distress caused by mutilating abdominal scars in women of whatever age who have to undergo gynaecological operations. Its plea for a nicer planning of laparotomy incisions in women deserves the widest attention. The author shows that the incision he describes gives ample access to the abdominal cavity for most forms of conservative gynaecological surgery and

for Caesarean section and the reviewer confirms his claims after considerable trial of his method. The appendix, too, is easily approached thus and it must be the hope of all of us that we might less often have to see the abdomen of a woman disfigured by those most unsightly of scars, the paramedian and the McBurney, which mark the trail of the appendisectomist.

The author traces precisely on the abdominal skin a transverse incision of not more than 10 cm. in length, within the pubic hair-line, slightly curved, with its centre about 4 cm. above the pubis. He assures its position and symmetry by placing on the abdominal wall a plate of thin metal hooked at either end to fit over the pubis and the umbilicus. The incision is traced with methylene blue through a linear perforation in the plate and symmetrical surture lines are traced through cross perforations. The skin is incised along this tracing. The aponeurosis can be incised at a slightly higher level giving an opening of up to 12 cm. long, and if further space be needed the lower flap is divided longitudinally and then dissected off the underlying muscle. The recti are separated and the peritoneum incised longitudinally. The author advises deliberation and careful haemostasis at all stages, allowing himself 15 minutes to complete the incision and introduce packs and retractors.

The reviewer commends the author's ideals and their mode of presentation in this book. The reader ignorant of Spanish will easily follow the argument from the excellent illustrations alone.

"Gestation Periods. A Table and Bibliography." Second edition. Compiled by J. H. KENNETH, M.A., Ph.D., F.R.S.E. Imperial Bureau of Animal Breeding and Genetics. Edinburgh, 1947. Pp. 30; price 3s.

THIS pamphlet provides, in tabular form, details of the lengths of the gestation periods of mammals— average, minimum and maximum. Each item has its reference to the literature. Altogether there are 442 such references. The second edition includes details of 35 additional species and 100 additional references. The pamphlet supplies a complete and ready source of reference to all concerned with the study of comparative reproductive biology.

"A Short Textbook of Midwifery." By G. F. Gibberd. (1947). J. & A. Churchill, London. Price 21s.

MR. GIBBERD's "Short Textbook of Midwifery" extends to 545 pages of letterpress. The arrangement of the contents is planned to present initially a complete picture of normal pregnancy and labour, including a discussion of occipito-posterior position and plural pregnancy, after which abnormalities of pregnancy are discussed, followed by separate consideration of mal-presentations, contracted pelvis, and faults in the forces of labour. Antepartum haemorrhage and abnormalities of the third stage next receive attention, and the book is then concluded by sections on the normal and abnormal puerperium, on obstetric operations, and on neo-natal paediatrics. The difficulties inherent in presenting the subject in this form have been tackled with skill. The book as a whole is readable and its continuity is well maintained.

Certain subjects receive a disproportionately thorough treatment in what purports to be a short textbook. For example the chapter on "Puerperal Infections" extends to 46 pages. This particular chapter, besides being the longest, is probably the ablest and most interesting in the whole book; but the detail in which the subject is considered is more worthy of a place in a highly specialized textbook than in one which is probably designed to meet the needs of the undergraduate and general medical practitioner.

Reading a textbook by this author one instinctively turns to the section on "Toxaemias of Pregnancy", where, however, a disappointment awaits, for, in discussing the nomenclature for the common late toxaemia of pregnancy, Mr. Gibberd decides that the term "Albuminuria of Pregnancy" is preferable to its synonyms, of which he lists "Pregnancy kidney, pre-eclamptic toxaemia, hypertensive toxaemia, and late toxaemia" It is regrettable that Mr. Gibberd should give his authority to the perpetuation of this unsatisfactory term. Furthermore, references to the common occurrence of a chronic nephritis as a sequel to pregnancy toxaemia might justifiably be dropped from a modern textbook. The discussion of the theories of aetiology of eclampsia is an admirable piece of verbal compression, but suffers somewhat from the absence of clearly-headed sub-paragraphs,

while reference to the possible influence of dietetic deficiencies is somewhat perfunctory.

In some general subjects it is good to see the emphasis placed upon the theories of unequal foetal flexibility in relation to internal rotation of the head; and the lucid summary of the uses of X-ray pelvimetry is useful. It is to be regretted, however, that there are so few illustrations to certain sections dealing with manual procedures. In a students' textbook, it is a bold but perhaps justifiable step to avoid illustrations of Caesarean Section (as Mr. Gibberd does), but to find that breech delivery is described in detail entirely without illustrations is very surprising. Such an omission puts a very unfair strain both on the concentration of the student and upon Mr. Gibberd's descriptive powers, outstandingly clear though these are.

The author makes use of a number of statistics in respect of the "Class A" patients at Guy's Hospital, hoping thereby to present figures for the incidence of various complications in an average and unselected population. This is an extremely valuable teaching expedient, which one would like to see emulated in other authoritative writings, in which the statistics are too often unfairly loaded by the use of hospital figures. There are one or two omissions from his statistical survey, however. One would like, for example, to have a clear guidance given to the student of the actual incidence of forceps delivery in the Class A patients, while it might be useful to record the frequency of primary uterine inertia.

Mr. Gibberd's prose style is incisive and lucid. The pedant's ear, however, will be shocked by the very infrequent lapse, e.g., the use of inapplicable adverbs, as in the statement that " excessive vomiting . . . is practically never fatal." It must also be confessed that one such pedant objects strongly to Mr. Gibberd's use of " Syncitium " as an alternative to " Syncytium ".

A review of a previous edition of Mr. Gibberd's textbook in this journal summed it up as an essentially " safe " textbook. With this the present reviewer would like to concur, adding that it is also well written, thoughtful, and interesting. Its value would be considerably enhanced by the inclusion of a very short bibliography at the end of each chapter, referring the earnest student to the original publications of the authors mentioned by name in the general body of the letterpress.

W. I. C. MORRIS

REVIEWS OF HOSPITAL REPORTS

MEDICAL AND CLINICAL REPORT OF THE SIMPSON MEMORIAL PAVILION, ROYAL INFIRMARY, EDINBURGH, FOR THE YEAR 1945.

THE report is presented in two parts—obstetric and paediatric. The obstetric section is devoted mainly to patients confined in the hospital, but there is a short summary of 657 district cases of which 13 were abortions. There was 1 fatal case in the district (0.15 per cent maternal mortality). This patient (aged 37, para. 3) had been treated for general debility during pregnancy with iron tonics. At term labour was uneventful but during the 30-minute third stage there was a mild degree of haemorrhage. One hour after delivery she collapsed, but improved with blood transfusion and sedatives. Twenty-four hours later she complained of sudden pain in the left side of the chest, collapsed and died. There was no autopsy. Death is ascribed to acute heart failure. In the absence of a history of heart disease the reader might, perhaps, think the third stage haemorrhage a contributory, if not the principal factor.

In-patients numbered 3,873 among whom there were 3,202 deliveries. This figure includes 49 patients who were admitted after delivery outside. There were 11 maternal deaths. Pyrexia occurred in 58 cases. The standard of morbidity is all fatal cases and all cases in which the temperature reaches 100.4°F. in any 2 of the bi-daily readings from the end of the first day until discharge from hospital or the end of the 21st day after delivery. The morbidity-rate was 2.2 per cent.

Numerical tables show briefly the essential particulars of the important complications of pregnancy and labour encountered and of the obstetrical operations performed. Then follow 3 pages of notes summarizing each maternal death. A comparative table shows the maternal mortality rates for all deliveries, Caesarean section, eclampsia and placenta praevia, the morbidity-rate of all deliveries, the interference-rate—forceps and Caesarean section, and the foetal mortality-rate in uncomplicated primigravid breech delivery for the years 1932–1945.

Single case data are given for contracted pelvis, eclampsia, multiple pregnancy, placenta praevia, cardiac disease, uncomplicated breech deliveries, and embryotomy.

Placenta praevia was encountered in 40 patients who gave birth to 41 babies. There was no maternal death. Of these 41 babies 12 appear to have been stillborn or died (not 13 as stated). Using this apparently erronous figure of 13 it is reduced to 4 on the grounds that 9 were under 36 weeks' maturity. The significant foetal survival-rate is thus claimed to be 87 per cent. (Actually by this means as only 12 babies do appear—from study of single case data—to have died the significant foetal survival-rate could be claimed as 90.6 per cent.) But the only reason for the elimination of these 9 premature babies is that they were dead. Seven other identical premature babies which lived are not excluded. The resulting figure is rather meaningless. It is the survival-rate of all babies of 36 weeks' maturity and over, and of those under 36 weeks' maturity which did not die, born to mothers who had placenta praevia. It would be reasonable to exclude babies who had a congenital deformity incompatible with life. There do not appear to have been any such babies. The foetal survival-rate in this whole series of placenta praevia cases is 70.8 per cent.

The foetal mortality in uncomplicated primigravid breech delivery is given as 10 per cent in a series of 50 cases. The reviewer would personally have eliminated 3 cases where the mother had toxaemia (in 2 the foetus survived and in 1 was stillborn); the corrected foetal mortality-rate would then be 8.5 per cent.

In 51 cases there was either retained placenta, adherent placenta or post-partum haemorrhage. Two patients died. Blood transfusion was given in 33 cases. The forceps delivery-rate was 11.6 per cent and the Caesarean section-rate 5.5 per cent—the maternal mortality-rate of 159 Caesarean sections was 1.98 per cent.

Maternal death occurred in 3 booked and 8 non-booked cases. Postpartum haemorrhage was the primary cause in 2 of the booked cases. In the first details given of the haemorrhage and its treatment are scanty. In the second forceps delivery under chloroform of the after-coming head in an assisted breech delivery was followed by a third stage haemorrhage and collapse. Blood transfusion was given: 2 days later she developed anuria which did not respond to intravenous infusions. She died in coma 6 days after delivery. Rh grouping is not mentioned. The third booked fatal case had toxaemia. She was delivered by Caesarean section under cyclopropane. Her condition was good throughout, but collapse occurred at the end of the operation. She died in spite of transfusion 3½ hours later. The amount of haemorrhage is not stated. Of the 8 emergency fatal cases toxaemia in a wide sense was the underlying cause. At least 7 would appear to have been unavoidable deaths as far as the hospital was concerned. Sepsis, as a major cause of maternal death, can now be controlled. Death from haemorrhage should be largely controllable. But here again as in report of hospital after hospital is the baffling toxaemia problem.

The paediatric section deals with the babies born during the year. The total was 2,730 live births and 132 stillbirths. There were 16 previable (under 2¾ pounds) infants—none survived. The neonatal death-rate was 30.8 per 1,000 live births for all infants (viable prematures 229.4, and mature infants 12.4 per 1,000 live births). At the end of 2 weeks or on discharge 78.1 per cent infants were wholly breast fed. 9.8 per cent infants displayed a morbid course. The causes of morbidity are tabulated. The cause of death was known in 88 out of 89 cases and was determined by postmortem in 71. The stillbirth-rate for all infants was 46.1 per 1,000 live births. The combined stillbirth and neonatal death-rate is 76.9 per 1,000 live births.

THE MEDICAL REPORT OF THE ROYAL SAMARITAN HOSPITAL FOR WOMEN, GLASGOW, FOR THE YEAR 1945.

THERE were 3,700 (corrected for readmissions) patients admitted to this gynaecological hospital. On them were performed 3,468 operations with a mortality of 0.70 per cent.

The bulk of the report consists of a table occupying 20 pages dealing with the pathological conditions encountered. These are tabulated on a regional basis, a general basis including errors of development, conditions resulting from infection, injuries, fistulae and displacements, diseases outwith the genito-urinary tract, and certain non-classifiable conditions. The number of cases is given and with this are correlated certain other facts such as the average age, parity, number married, etc.

A brief summary is given of 26 fatal cases. Nine of these deaths resulted from operations for genital prolapse: 3 are ascribed to shock, 2 to widespread sepsis, 1 to pulmonary embolism, 1 to heart failure 14 days after operation, 1 to acute pyelonephritis while 1 (a diabetic) died in diabetic coma 24 days after operation. It is not possible to calculate the mortality-rate for these plastic operations as the number done is not stated. The number of major vaginal operations performed is given as 486. One abdominal operation and 1 major vaginal operation were performed on the same patient. If we assume that an operation for genital prolapse is a major vaginal operation, and that every major vaginal operation performed in the hospital during the year 1945 was for genital prolapse then the hospital's mortality for prolapse operations is 1.84 per cent. There were 2 anaesthetic deaths: 1 further patient died without regaining consciousness from the anaesthetic after a diagnostic curettage—autopsy revealed chorion-epithelioma with distant metastasis. Four deaths were associated with malignant disease and 1 with congenital heart failure.

A brief description is given of the modified Paris technique employed in the treatment of cervical uterine cancer. Details are given too of the patients receiving deep X-ray therapy, for both benign and malignant conditions, since 1938 with follow-up figures. These figures will be of interest to those who study the results of malignant disease of the female genital organs.

OBSTETRICAL AND GYNAECOLOGICAL REPORT OF THE ROYAL VICTORIA HOSPITAL, MONTREAL, CANADA.

This is a combined report for the 2 years ended December 31st, 1944 and 1945. The total number of beds in the obstetric and gynaecological departments is not stated but the number of patients cared for during these 2 years is large. There were 9,387 adults and 4,759 children—a total of 14,146 patients.

In the obstetric department there were 5,461 in-patients of whom 5,288 were booked and 173 emergency cases. The total number of confinements in the hospital was 4,869 of which some 24, occurring before the 28th week, were abortions. Single case data are given only for adults and infants transferred to other departments, and for maternal deaths. The rest of the report is numerical.

Maternal death did not occur in any case of Caesarean section which was performed on 219 occasions although there was a foetal mortality of 26 (11.8 per cent). Spinal anaesthesia was employed in 203 cases and local in 16 cases. Quite apart from the question of the anaesthetic agent the maternal result is most satisfactory. Doubtless both the protagonists and antagonists of spinal anaesthesia for Caesarean section will be interested in these figures.

The section dealing with infant mortality is perplexing. The deaths are divided into " full-term " (which is an understandable term) and " premature (28 weeks)" (which is not as thus defined an understandable term). In both of these classes a distinction is drawn between " born dead (antepartum, and intrapartum)", " stillborn ", and " died postpartum." Careful study of this table fails to reveal any undefined subtle difference between stillborn and born dead. Undefined, such a distinction is confusing and of no value. It should be eliminated.

The standard of obstetrical morbidity used is a single rise in temperature to 100.6°F. (after the first 24 hours and until discharge). The morbidity-rate, the lowest in the hospital's history, was 16.8 per cent.

The maternal mortality-rate, 0.08 per cent, is the result of 5 deaths. In 3 eclampsia or toxaemia was the cause of death—they were emergency admissions, in terminal condition, and had had no antenatal care at all. In 1 death was due to post-partum haemorrhage 2 hours after a low forceps delivery: labour had lasted 72 hours. Manual removal of the placenta at the time of delivery might possibly have prevented this death. The fifth death was due to ruptured uterus, retro-peritoneal and intraperitoneal haemorrhage in a case of breech presentation with hydrocephalus in which craniotomy was employed.

A special toxaemia clinic, by which all toxaemic patients on the public services were treated, is considered to have justified itself. Educational classes in personal hygiene, food requirements and infant care held in the out-patient department speak for the progressive direction of the obstetrical department.

In the gynaecological department there were 3,926 admissions. There were 7,640 out-patient attendances of which 1,881 were new visits. A broad classification with numerical incidence of non-malignant diseases is given. (Malignant disease is dealt with in the Radium Clinic Report.) The list of operations performed presents no unusual feature. Local colour is given by the performance of Dr. Chipman's operation 348 times out of 450 operations for the cure of sacro-pubic hernia.

Of 27 deaths 16 were associated with malignancy. Of 11 deaths from non-malignant conditions 2 were due to blood transfusion, 3 to pulmonary embolism of which 2 occurred in women under 40 on whom plastic repair for prolapse had been performed, while 1 succumbed to air embolism during tubal insufflation for sterility.

The report closes with that of the Radium Clinic. This includes an excellent summary of the results of cervical and corporeal uterine cancer treated by radium for the years 1926 to 1945.

MEDICAL AND CLINICAL REPORT OF THE WOMEN'S HOSPITAL, CROWN STREET, SYDNEY,

From 1st July, 1944, to 30th June, 1945.

THIS report deals with the patients in the public wards of the hospital. The in-patients are accommodated in one of three departments. These are the Indoor Maternity, the Founders' Block (Isola-

tion) and the Gynaecological departments. In these there were 4,326, 924 and 410 patients respectively during the year. Confinements in hospital numbered 3,616, and on the district 49. The out-patient attendances were large—36,796 adults and 1,056 babies.

In the maternity department there were 3 deaths among booked patients and 6 among emergency cases, making a total of 9 deaths. In the first booked case death was ascribed to acute hepatic necrosis: labour was induced for toxaemia, delivery was instrumental: death occurred 2 days later. The second died of pulmonary embolism following hysterotomy and sterilization for hypertension (250/140) and albuminuria in a pregnancy of 24 weeks' duration. The third death was primarily due to postpartum haemorrhage: a 6-gravida, aged 29, was delivered of a 7½ pounds infant after a normal labour of 1½ hours; a 10-minute third stage was followed by a profuse haemorrhage which was controlled to slight bleeding " and exploration of cervix with speculum showed this to be coming from above os. Blood transfusion continued but, as some bleeding continued, manual exploration of uterus and *laparotomy performed* [reviewer's italics]. As bleeding was still free 2½ hours later, uterus and vagina were packed with gauze. This was removed 36 hours later and patient's condition was satisfactory. She died suddenly from pulmonary embolism on the sixth day of puerperium." It is to be regretted that details of a case so interesting, and probably most instructive, are incomplete. Why the laparotomy? What was found? What was done? In 3 of the deaths among emergency cases toxaemia (2 with eclampsia) appears to be the prime cause. Of the 3 remaining, 1 died of acute appendicitis with general peritonitis; 1 (aged 18) of acute hepatic necrosis and uterine infection following prolonged labour, failed forceps outside and difficult delivery in hospital. The last (primigravida of 24), admitted in poor condition with an impacted breech and history of outside interference, was delivered with difficulty by blunt hook and perforation of aftercoming head. "*Later* [reviewer's italics] manual removal of placenta. Patient was very shocked and died about 14 hours later." What was the length of the third stage? How much haemorrhage accompanied it? Was an additional anaesthetic given for the manual removal? We all meet these difficult cases. Would that the published reports gave full details!

The tables of single case data of complications deserve study. There were 29 cases of placenta praevia. No mother died. But the foetal mortality was 72.4 per cent. On 8 occasions central placenta praevia was treated by version and bringing down of a leg: on each occasion the baby was stillborn.

Caesarean section was performed on 5 occasions but only 2 of the babies survived. Postpartum haemorrhage occurred 241 times (6.6 per cent). Forceps was used 414 times (11 per cent). Caesarean section was performed 34 times (0.9 per cent) without any maternal fatality. The morbidity-rate for the whole obsteric department was 5.6 per cent. This figure cannot be regarded as reliable. The standard of morbidity is said to be that of the British Ministry of Health namely " a temperature of 100.4°F. in the first days of the puerperium, sustained for 24 hours or recurring during that period." It will be observed that this is not the British Ministry of Health standard but a paraphrased version of it, even more ambiguous than the much maligned standard itself.

Stillbirths numbered 124 (27 macerated) which is 33.9 per 1,000 births. If premature and nonviable infants are excluded the corrected rate is 22 per 1,000 births at term. Neonatal deaths numbered 102, i.e., 28 per 1,000 live births; excluding premature and non-viable infants the corrected rate would be 11 per 1,000 live births. The combined stillbirths and neonatal deaths numbered 226, i.e., 61.9 per 1,000 births. This figure can be corrected as the two former to 29.8 per 1,000 births.

Of 283 premature (5½ pounds or less) babies born alive 65 (23 per cent) died. Each stillbirth and neonatal death is set out singly. Autopsy was performed on 102 infants.

From the Founders' Block—Isolation wards and "E" wards—924 or 925 patients were discharged. Of these 835 suffered from some variety of abortion. Patients admitted over 28 weeks pregnant or after delivery of a " viable " infant are not included in these figures, but are dealt with in the Indoor Maternity Report. Among the 900-odd patients there were 5 deaths. Three died of postabortional sepsis—one due to Cl. Welchii. One aborted incompletely while undergoing treatment with Lugol's iodine for thyrotoxicosis. The uterus was

curetted under nitrous oxide anaesthesia. One week later she underwent operation for sterilisation. She died 40 hours later from auricular fibrillation and hyperpyrexia. The last (aged 37, fifth gravida), admitted with congestive heart failure and anaemia (Hb. 53 per cent) at 20 weeks' pregnancy, was given a successful drug induction when the maximum expected recovery had taken place. Unexpectedly she became maniacal and died from exhaustion.

From the Gynaecological Department 410 patients were discharged. There were 2 deaths.

One (aged 66) died from intestinal obstruction some days following radium treatment for confirmed carcinoma corporis uteri. The other (aged 34) died of meningitis (B. proteus) a few days after a Fothergill operation for uterine prolapse. The gynaecological conditions dealt with and the operations performed are enumerated.

Brief reports are given of the work of the pathological and X-ray departments, the sterility clinic, the mobile blood transfusion unit, and the Almoner's department.

Anthony W. Purdie

REPORTS OF SOCIETIES

ROYAL SOCIETY OF MEDICINE
(Section of Obstetrics and Gynaecology)

Meeting held on Friday, February 21st, 1947.

THE evening was devoted to short communications and descriptions of cases by the registrars of hospitals in London and the Home Counties. Dr. Elliot Philipp, Middlesex Hospital, described the treatment of tuberculous salpingitis with special reference to X-ray therapy. Thirteen cases in a series had been treated with X-rays, 12 of them had had laparotomy performed, and 5 had developed a tuberculous sinus following the operation. Within 6 months of the start of X-ray treatment all the sinuses had healed. Treatment involved the giving of very small doses—a total of about 600 r in a course of 12 to 18 treatments, spread over 6 to 9 weeks. From all these cases the only conclusion that could be drawn was that there was as yet no fixed rule for the treatment of tuberculosis in the pelvic organs. Emphasis was put on the importance of rest, good food, heliotherapy, and possible radical surgery.

Dr. Ian Donald, St. Thomas's, described an investigation he had made into the incidence of difficulties in the third stage of labour following the use of Pethidine. His investigations were stimulated by what he termed "a bad run" of

manual removal of the placenta. Although only a relatively small number of cases were available, he was able to come to the conclusion that the danger of postpartum haemorrhage could not be ascribed to the use of this substance in the earlier stages of labour.

Mr. Ian Fraser and Dr. Karnicki described cases of full-time ectopic pregnancy. That described by the latter was most remarkable in that a living baby, who survived, was delivered at operation. Dr. Lois Hurter described a case of dysgerminoma of the ovary in a girl of 15. Dr. D. R. Kilgour described a case of carcinoma in the body of the uterus. Dr. R. W. Danziger showed an enormous fibrolipoma, which had grown rapidly from the vulva in a young woman.

Mr. M. Hemans drew attention to the incidence of endometriosis of the cervix. Dr. M. Donald gave the Section a description of a remarkable case of rupture of the uterus. In this patient the uterus ruptured with the final contraction that gave birth to the child, which fact led to considerable difficulty in the making of a diagnosis.

H

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

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By H. THOMS. *Yale J. Biol. Med.,* **19,** 171–179, Dec., 1946. 10 figs., 8. refs.

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By G. DUBREUIL and M. RIVIÈRE. *Gynécologie,* **43,** 97–127, July–Aug., 1946. 11 figs., 4 refs.

218. Morphology and Histology of the Corpus Luteum. Processes of Degeneration and Remains. (Morphologie et histologie des corps progestatifs et gestatifs (corps jaunes) de l'ovaire féminin. Modes de dégénérescence et reliquats.)

By G. DUBREUIL and M. RIVIÈRE. *Gynécologie,* **43,** 129–179, Sept.–Oct., 1946. 12 figs., 125 refs.

PHYSIOLOGY

219. Histophysiology of the Endometrium; Spiral Arterioles and their Function. (Contribution à l'histophysiologie de l'endomètre. Les artérioles spiralées. Leur fonction. (Première note).)

By P. ISIDOR. *Gynécologie,* **43,** 193–199, Nov.–Dec., 1946. 10 refs.

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By F. v. MIKULICZ-RADECKI. *Med. Klinik.,* **41,** 446–448, Oct., 1946. 1 fig.

221. Does the Ovary Present Cyclic Variations During Pregnancy? (L'ovaire présente-t-il des variations cycliques pendant la gestation?)

By E. BUJARD. *Rev. méd. Suisse rom.,* **66,** 763–769, Nov. 25, 1946. 16 refs.

222. Chronaximetric Estimation of Hormones in Gynaecology and Obstetrics. (Courte note sur l'utilisation en gynécologie et en obstétrique de capachronaximètre: dosage chronaximétrique des hormones.)

By J. COURTOIS. *Gynécologie,* **43,** 211–212, Nov.–Dec., 1946. 2 refs.

223. Pregnandiol Determinations Made During Last Days of Gestation. [In English.]

By T. DAHLE. *Acta obstet. gynec. Scand.,* **26,** 627–632, 1946. 4 figs., 4 refs.

Pregnandiol determinations in the urine of 4 pregnant women have been carried out during the last days before delivery. Any noticeable reduction in the pregnandiol secretion has not been proved.—[Author's summary.]

224. The Effect of Thiouracil Hypothyroidism on Reproduction in the Rat.

By G. E. S. JONES, E. DELFS, and E. C. FOOTE. *Endocrinology,* **38,** 337–344, June 1946. 2 figs., 2 refs.

Fourteen male and 15 female adult rats had their drinking water replaced by 0.1 per cent thiouracil solution: the average daily intake of the drug was 24 mg. in the males and 20 mg. in the females. Treatment was continued for from 49 to 340 days, and thyroid hyperplasia was produced in all cases. The increase in thyroid weight was greater in the males; the highest weight was 170 mg., against 42 mg. in the females.

Six male rats successfully sired litters after 49 days' treatment, but of 16 attempted matings after 166 to 259 days treatment only 8 were successful. The failures could, however, be attributed to illness, or were in rats which mated successfully in later attempts. There appeared to be some prolongation of the gestation period, which averaged 31 days, excluding two of 57 and 94 days. [No control data of mating or gestation records for the colony are given.]

Nine females treated for 84 days all mated successfully, but 4 resorbed their litters; resorption of litters occurred in all of 18 matings made after 126 to 202 days of treatment.

While the upsets in male fertility are attributed to the general toxic effects of the drug, the resorption of the litters in the females is attributed to the induced hypothyroidism. The mechanism of this effect is discussed, and it is suggested that faulty utilization of oestrogen and / or progesterone in thyroid deficiency leads to a relative deficiency of one or both so that pregnancy cannot be maintained.

Peter C. Williams

225. Our experience with Falls-Freda and Cohen's Intradermal Reaction for the Diagnosis of Pregnancy. (Nuestra experiencia con la intrader mo-reaccion calostral de Falls-Freda y Cohen, para el diagnostico del embarazo.)

By D. T. GOROSTIAGA and R. E. LEDE. *Rev. Med. Cien. af.,* **8,** 870–872, Nov. 1946, 5 refs.

226. Prenatal Examination. (Examen prénatal.)

By D. MARION. *Union méd. Can.,* **75,** 1372–1379, Nov. 1946. 1 ref.

227. Prenatal Medical Examination. (L'examen médical prénatal.)

By E. COUTURE. *Union méd. Can.,* **75,** 1604–1608, Dec. 1946.

228. **The Management of the Toxaemias of pregnancy.**

By J. S. BREWER, G. M. COOPER, E. W. FRANKLIN, J. S. HUNT, T. L. LEE, I. PROCTER, R. A. ROSS, R. A. WHITE, and F. R. LOCK. *North Carolina med J.*, 8, 31–34, Jan. 1947. 1 fig.

229. **Psychosis in Eclampsia.** (Psicosis eclamptica.)

By F. PEREZ ACOSTA. *Rev. méd.-quirúrg. Oriénte.*, 7, 147–153. Sept. 1946.

230. **Use of Spasmolytic Drugs in Eclampsia.** (El uso de espasmoliticos en la eclampsia.)

By E. RODERIGUEZ NUNEZ. *Rev. méd. Cubana*, 57, 626–634, Aug. 1946. 7 refs.

231. **Pathogenesis and Mechanism of so-called Toxic Accidents in Pregnancy.** (Contribution à l'étude de la pathogénie et du méchanisme des accidents dits "toxiques" de la gestation.)

By J. GRASSET. *Rev. franç. Gynéc.*, 41, 369–393, Dec. 1946.

232. **The Management of Placenta Previa at the Chicago Lying-in Hospital. A Review of 325 Cases during 1931 to 1945.**

By M. E. DAVIS and A. CAMPBELL. *Surg. Gynec. Obstet.*, 83, 777–788, Dec. 1946.

A careful and detailed summary of a considerable number of cases of placenta praevia treated over a period of years in a large hospital can generally be studied with interest and profit even though, as must usually be the case, no particularly novel or original views as to methods of diagnosis or management are expressed. In this report the management of 325 cases during the years 1931 to 1945 is reviewed. In this series there were only 2 maternal deaths: 1 from haemorrhage shortly after Caesarean section, the other 16 days after operation from sepsis and pulmonary complications—a mortality of 0.6 per cent. The following points are emphasized. There is no treatment of placenta praevia that can be carried out at home; all patients with antepartum haemorrhage after the twenty-eighth week should be admitted to hospital. Vaginal examination should be made only in surroundings where blood transfusions and operative treatment are immediately available. Lower-segment Caesarean section is the best treatment for all cases of central placenta praevia. This operation was done in 121 cases—63 of central and 58 of partial and marginal placenta praevia. The Porro operation was performed for 15 cases. In most cases of incomplete placenta praevia delivery can be completed through the birth passages. Rupture of the membranes is the method of choice, sometimes combined with the use of Willett's forceps (11 cases). Version was performed 15 times, and the bag was inserted 48 times, though the authors now believe that both these methods should be discarded. Tamponade has no place in the treatment. The value of blood and plasma transfusions, supplemented sometimes by intravenous saline, is stressed, as is the importance of having Rh-negative blood or a donor available.

T. C. Clare

233. **A Case of Utero-placental Apoplexy and Placenta Praevia.** (Sobre um caso de apoplexia útero-placentária e placenta prévia.)

By C. VIEIRA. *Rev. Ginec. Obstet.*, 2, 188–192. Sept. 1946.

234. **Fifty Cases of Induced Abortion with Reference to the Follow-up of Treated Patients.** (50 Tilfaelde af Abortus provocatus med særligt Hanblik paa Efterundersogelse af de afviste Tilfaelde.)

By G. KRALUND. *Ugeskr. Læg.*, 108, 1401–1403, Dec. 12, 1946. 1 ref.

235. **Induced Abortion.** (Abortus provocatus.)

By M. A. VAN B. BASTIAANSE. *Tijdschr. soc. Geneesk.*, 25, 53–61, Feb. 28, 1947.

236. **Embolism after an Attempt at Abortion.** (Apropos d'une embolie après manoeuvre abortive.)

By —. HIRSCH and —. DE TOEUF. *Brux. Méd.*, 27, 164–168, Jan. 26, 1947. 22 refs.

237. **Hydatidiform Mole versus Chorionepithelioma.** (Môle hydatiforme vs chorioepithéliome.)

By L. GERIN-LAJOIE. *Union méd. Can.*, 75, 1380–1383, Nov. 1946.

238. **Fibroma and Pregnancy.** (Fibrome et grossesse).

By A. MARMEAUX. *J. Méd. Paris*, 67, 21, Feb. 1947.

239. **A Case of Chorioepithelioma.** (Corioepithelioma – Caso clínico.)

By L. MAYORGA. *Bol. Soc. chil. Obstet. Ginec.*, 11, 136–141, Sept. 1946. 3 figs.

240. **A Case of Perforating Chorioepithelioma with Haemoperitoneum.** (Corio-epitélioma perforante. Hemo-peritoneo. Caso clínico.)

By J. ALLAMAND and A. LUCCHINI. *Bol. Soc. chil. Obstet. Ginec.*, 11, 133–136, Sept. 1946. 5 refs.

241. **Diagnosis and Treatment of Uterine Rupture.** (Diagnóstico y tratamiento de las rupturas uterinas.)

By H. CAICEDO DIAZ. *Med. Cirug.*, 11, 33–44, Nov. 1946.

242. Cerebrovascular Complications of Pregnancy. By W. C. ELLER. *Amer. J. Obstet. Gynec.*, 52, 488–491, Sept. 1946. 1 fig., 3 refs.

Cerebrovascular complications of pregnancy deserve attention because: (1) gross brain haemorrhage is found in 15 to 20 per cent of necropsies after eclampsia; (2) appreciable brain haemorrhage has a mortality of over 50 per cent and is the second commonest cause of death in eclampsia; (3) areas of softening (encephalomalacia) are relatively frequent, are often unrecognized, and may cause death in the absence of haemorrhage; and (4) patients with sufficient vascular damage to produce fatal haemorrhage or softening should not always be diagnosed as cases of " eclampsia ", even in the presence of hypertension, albuminuria, oedema, and convulsions. Three cases are reported.

The first patient, aged 36 years, gravida 9, para 6, had had no antenatal care and was admitted in labour. She had had " fits " with her first pregnancy, but gave no history of hypertension or renal disease; blood-pressure was 195/92, and there was moderate ankle oedema with a trace of albuminuria and a few red-blood cells in the urine. There was uterine inertia. In the next 21 hours she received 2 litres of 5 per cent dextrose in water and sedation with morphine and scopolamine, but the blood-pressure remained elevated, and the temperature rose to 102°F. (38.9°C.); 1 litre of 5 per cent dextrose in water was given by hypodermoclysis. Pulmonary oedema developed, and the patient died in coma 31 hours after admission. Postmortem examination showed generalized slight arteriosclerosis, medial necrosis of the thoracic aorta, perivascular haemorrhage throughout the brain, and an area of 2 cm. in diameter of encephalomalacia in the hypothalmus.

The second patient, a primigravida, had had no antenatal care, and was in labour on admission. She gave no history of hypertensive or renal disease. Blood-pressure was 220/156 and oedema and considerable albuminuria were present. She was delivered spontaneously 4½ hours later of a child weighing 3,041 g. (6 pounds 11 ounces). Blood-pressure fell during labour, but rose 12 hours later, reaching 220/150. Convulsions 19 hours after delivery preceded coma and Cheyne-Stokes respirations with a temperature of 105°F. (40.6°C.). Left hemiplegia and right oculomotor palsy developed. The spinal fluid was under a pressure of 152 mm. of water, contained 188 red blood cells per c.mm. and 224 mg. of protein per 100 ml. The patient died in coma 92 hours after delivery. Postmortem examination revealed a large area of haemorrhage and encephalomalacia in the right mid-brain at the level of the red nucleus just anterior to the cerebral aqueduct and extending to the lower portion of the pons beneath the floor of the fourth ventricle, with very little evidence of chronic arteriolar or renal disease.

The third patient, aged 39 years, para 1, had been treated 2 years previously for a " stroke " and high blood-pressure. It was stated that she complained of pain in the left arm before she fell to the floor. On admission she was comatose; blood-pressure was 246/130; reflexes were equal but hyperactive; the right eye looked down and out. There was no oedema, but there was albuminuria with occasional red blood cells. The spinal fluid was clear under a pressure of 220 mm. of water, with 100 mg. of protein per 100 ml.; later the pressure rose and macroscopic blood appeared. Reflexes gradually disappeared, and hyperpyrexia developed. She died 28 hours after admission. Postmortem examination revealed generalized arteriosclerosis, nephrosclerosis, and cardiac hypertrophy. There was an area 3 cm. in diameter (with surrounding encephalomalacia of indefinite extent) of recent haemorrhage in the mid-brain just above the pons. This patient, in whom the findings and clinical course were similar to those in the other 2 cases, was not pregnant.

Normal blood vessels can withstand a very high pressure over a long period. So with vessel disruption sufficient to produce gross haemorrhage a pre-existing lesion of the vessel wall (such as is seen in essential hypertension, vascular syphilis, or congenital aneurysm) might be expected. But in true pre-eclampsia and eclampsia reversible vasospasm is the only vascular lesion. The third case illustrates the fact that the chronic vascular changes are not peculiar to pregnancy. The second patient showed none of these chronic vascular changes. It is suggested that the temporary vasospasm produces an area of softening distal to the point of spasm. In the area of softening thus produced the vessel itself may undergo softening and subsequent disruption and haemorrhage. At any rate, encephalomalacia itself of sufficient extent or in a suitable place may have a fatal result. The

importance of neurological examination in the toxaemic patient is stressed. This point is not purely academic. Certain intracranial haemorrhages are amenable to possible life-saving surgical treatment.   *Anthony W. Purdie*

243. **Pyeloureteritis in Pregnancy.** (Pieloureteritis gravidica.)

By A. J. GUIROY and F. A. URANGA IMAZ. *Prensa med. argent.*, 34, 97–102, Jan. 10, 1947.

244. **Impregnation, Pregnancy and Diabetes.** (Fecundación, embarazo y diabetes.)

By M. ESPEJO and G. DE AVELLANEDA. *Actualid. méd. Granada*, 22, 705–708, 1946.

245. **Heart Disease in Pregnancy.**

By B. E. HAMILTON. *J. Missouri med. Ass.*, 44, 17–21, Jan. 1947.

246. **The Heart and Vitamin B₁ Deficiency in Pregnancy.** (Cuore ed ipovitaminosi B₁ in gravidanza.)

By F. DE MATTEIS and E. ROBECCHI. *Minerva med. Torino*, 1, 201–204, Feb. 17, 1947. 3 figs.

247. **Coarctation of the Aorta in Pregnancy.** (Isthmusstenose en zwangerschap.)

By G. A. LINDEBOOM. *Ned. Tijdschr. Geneesk.*, 91, 155–157, Jan. 18, 1947. 4 refs.

248. **Chylothorax: Pregnancy in an Arrested Case.**

By G. EDLUND *Minn. Med.*, 30, 47–48, Jan. 1947. 5 refs.

249. **The Action of Penicillin on the Guinea-Pig Uterus.** (Action de la pénicilline sur la corne utérine du cobaye.)

By J. PELLERAT and —. MURAT. *Ann. Derm. Syph.*, 6, 363–364, May–June, 1946. 1 ref.

The possibility of abortion due to the action of penicillin on the pregnant uterus has been suggested, as in pregnant women treated with penicillin for gonorrhoea spasmodic uterine pains have been reported. Penicillin in a dose of 0.5 units per ml. was found to cause contraction of the isolated guinea-pig uterus, whereas this dose has no action on the isolated intestine. The concentration of penicillin which produces uterine contractions *in vitro* corresponds to that obtained in the blood *in vivo* after an intramuscular injection of 20,000 units.   *G. M. Findlay*

250. **Origin, Course and Symptomatology of Intraligamentous Pregnancy.** (O postanku, razvitku i simptomatologiji intraligamentoznog graviditeta.)

By F. DRAZANCIC. *Lijecn. Vjesn.*, 68, 227–232, Dec. 1946. 2 figs., 15 refs.

251. **Vesical and Renal Symptoms in Interrupted Extrauterine Pregnancy.** (Sintomi vescicali e sintomi renali nella gravidanza extrauterina interrotta.)

By B. SORRENTINO. *G. ital. Chir.*, 2, 539–550, Dec. 1946. 3 figs., 10 refs.

252. **Repeated Ectopic Pregnancy.**

By H. BRYAN and T. J. MONTEMURO. *Canad. med. Ass. J.*, 55, 601–602, Dec. 1946. 3 refs.

253. **Two Cases of Interstitial Ectopic Pregnancy.** (Sobre dois casos de gravidez ectopica intersticial.)

By H. MACHADO HORTA. *Rev. Ginec. Obstet.*, 40, 296–301, Nov. 1946. 3 figs.

254. **Vagitus Uterinus. Report of Two Cases.**

By G. A. BOURGEOIS and H. L. KING. *Bull. U.S. Army med. Dept.*, 7, 147–148, Jan. 1947. 1 fig., 2 refs.

LABOUR

255. **Prognosis in Labour.** (Pronostico del parto.)

. By D. J. MILLAN SANTOS. *Toko-ginec. pract.*, 5, 371–380, Nov. 1946.

256. **Use of Calcium-quinine in Clinical Obstetrics.** (El empleo de la quinina-calcio en la clinica obstetrica.)

By J. BOTELLA LLUSIA, A. PEREIRA MARTINEZ, and J. GARCIA DEL ALAMO. *Medicina, Madrid*, 14, 361–392, Nov. 1946. 29 figs., 28 refs.

257. **Polycystic Disease of Kidneys Causing Dystocia. Review of the Literature and Report of a Case.**

By J. W. BOURLAND. *Urol. cutan. Rev.*, 50, 669–670, Nov. 1946. 8 refs.

258. **Foetal Ascites Obstructing Labour.** (Foetaler Ascites als Geburtshindernis.)

By K. MAGYAR. *Gynaecologia*, 122, 363–370, Dec. 1946. 6 figs.

259. **Sympatheticomimetic Amines in Labour.** (Le amine simpaticomimetiche nel travaglio del parto.)

By G. P. BALASSI. *Ginecologia, Torino*, 12, 297–306, Oct. 1946. 34 refs.

260. **Results of the Use of Compositrine in Connection with Danger to the Foetus.** (Uitkomsten van het gebruik van compositrine [ermetrine compositum] bezien in verband met gevaren voor het kind.)

By B. S. TEN BERGE and G. LINTHORST. *Ned. Tijdschr. Geneesk.*, 90, 1723–1731, Nov. 23, 1946. 2 figs., 6 refs.

261. **Management of Breech Delivery.** (Acerca da assistência ao parto de nádegas.)

By M. QUEIROZ DE BARROS. *Rev. Ginec. Obstet.* 2, 143–153, Sept. 1946. 2 figs., 52 refs.

262. **Bracht's Method in Breech Presentation.** (La maniobra de Bracht en el parto podálico. [Nota previa sobre una experiencia personal de 26 casos].)

By N. O. DI FONZO. *Rev. méd.-quirúrg. Pat. fem.*, 25, 392–399, Sept. 1946. 4 figs., 9 refs.

263. **Prognosis and Management of Labour in Breech Presentation in Cases of Pelvic Contraction.**

(Prognosi e terapia del parto in presentazione poda-lica nei bacini limite.)

By P. L. BIANCHI. *Ginecologia, Torino*, 12, 307–322, Oct., 1946. 20 refs.

264. **Transverse Presentation.**

By J. T. COLE and F. DELANY. *Surg. Gynec. Obstet.*, 83, 473–479, Oct., 1946. 18 refs.

The authors report 78 cases of persistent transverse presentation occurring in 45,000 deliveries at the Women's Clinic of the New York Hospital between 1932 and 1946. Their purpose is to present a recent series of cases and to evaluate the influence of advances in surgery, chemotherapy, and blood transfusion in the choice of treatment. Their series differs from others in that in as many as 46 per cent of cases delivery was by Caesarean section, with no maternal or foetal deaths. The paper opens with a short review of well-known papers on treatment from the mid-eighteenth century down to recent years. Then comes a brief account of the probable aetiological factors in the authors' series. One maternal death (1.3 per cent) and 18 foetal deaths (23 per cent) occurred in the whole series. Investigation revealed that 7 foetal deaths occurred before the onset of labour, 8 were associated with labour and delivery, and 3 were neonatal deaths. In the 58 cases in which the foetal heart was audible on admission and the foetus weighed 2.5 kg. or more only 5 foetal deaths occurred (8.6 per cent). The one maternal death (associated with placenta praevia and ruptured lower segment) is recorded in detail. Treatment is discussed at some length. The high mortality figures (both maternal and foetal) that accompany delivery from below, and the complications that arise from unwise internal version and breech extraction, are emphasized. The intelligent evaluation of the individual case must, naturally, always be made; but, in the authors' view, the more frequent use of Caesarean section is indicated by the low mortality figures.

[The authors present their evidence well and argue their case clearly. The fact is inescapable that modern technical advances have greatly increased the safety of Caesarean section and have justifiably widened its indications.]

Eardley Holland

265. **Uterine Inversion.** (Inversão uterina toco-genética.)

By F. COTTA PACHECO. *Rev. Ginec. Obstet.*, 2, 164–186, Sept. 1946. 5 figs., 24 refs.

266. **Post-partum Intra-abdominal Separation of Uterus.**

By J. J. S. WASSENAAR. *Brit. med. J.*, 1, 452, Apr. 5, 1947. 1 fig.

ANAESTHETICS, ANALGESICS

267. **Anaesthesia and Analgesia in Childbirth.**

By C. R. S. COLLINS. *J. nat. med. Ass.*, 39, 26–31, Jan. 1947. 15 refs.

268. **Local Infiltration Anaesthesia in Obstetrics and Gynaecology.** [In English.]

By J. P. GREENHILL. *Gynaecologia*, 122, 309–326, Dec. 1946. 5 refs.

269. **Continuous Spinal Anaesthesia in Obstetrics.**

By R. E. GILLETT. *Northw. Med.*, 45, 743–747, Oct. 1946. 24 refs.

The author's technique of continuous spinal analgesia in labour is described. The third or fourth lumbar interspace is selected for lumbar puncture. After preliminary puncture of the skin with a Sise introducer a malleable spinal needle is introduced; it is then fixed to the skin with strips of adhesive tape and allowed to remain *in situ*. Gauze soaked in antiseptic solution is wrapped around the shaft of the needle and the latter is connected by rubber tubing with a stopcock and syringe containing the anaesthetic agent. A special mattress provided with a cut-out space which accommodates the needle and tubing and allows the patient to lie on her back is essential. Anaesthesia is usually started as soon as uterine contractions are well established and pain is sufficient to justify its use. Pethidine intramuscularly or a barbiturate by mouth reduces apprehension, and 50 mg. of ephedrine by intramuscular injection is given prior to lumbar puncture.

" Pontocaine " (amethocaine hydrochloride) was used in 450 cases and "metycaine" in 50, and both were mixed with 10 per cent dextrose solution to produce a hyperbaric solution. The concentration of drug in each millilitre of this mixture was either 2 mg. of pontocaine or 15 mg. of metycaine. The volume of each injection was usually 2 ml., but in some instances this amount was increased to 3 ml. or reduced to 1 ml. All injections were made slowly and without barbotage and the height of anaesthesia was controlled by varying the position of the patient. The length of anaesthesia was readily prolonged by repeating the injection as required. Pulse-rate and blood-pressure were taken

at 5-minute intervals for the first half-hour following injection. The urinary bladder was observed, and catheterized immediately if it showed signs of distension. The spinal needle was removed before the patient was placed in her final position for delivery. A small injection gave adequate anaesthesia for delivery. Caesarean section could be performed under the same analgesic. Contraindications were: (1) Low blood-pressure; systolic 90 mm. and diastolic 50 mm. were considered the lowest limits. (2) Marked anaemia or actual or potential haemorrhage. Disease of the nervous system, infection at the site of contemplated puncture, emotional instability, or fear of spinal analgesia must also be considered.

Satisfactory analgesia was obtained in 95 per cent of cases. Only 1 case in 5 was delivered without some form of operative intervention. Episiotomy was performed in over two-thirds of the cases. No deaths were attributable to the analgesic. In only 36 per cent of cases was the drop in blood-pressure insignificant. Treatment was by injection of 4 minims (0.25 ml.) of 1 : 1,000 adrenaline solution in one case where the blood-pressure fell to zero. In the less severe cases of hypotension repeated intravenous ephedrine was found effective; the quantity and frequency of injections are not stated. The average duration of analgesia was 3½ hours for multiparae and 5 hours for primiparae; the longest was 24 hours.

John Challis

270. **Caudal Analgesia for Obstetrics in Private Hospital.**
By J. D. KINDSCHI. *Northw. Med.*, 45, 747–750, Oct. 1946. 3 refs.

Initial trials with caudal analgesia were unsatisfactory owing to faulty technique of needle insertion. Unilateral anaesthesia, drop in blood-pressure, and other discouraging results were obtained, and out of 15 cases only 3 were successful. In a series of 275 cases there were 5 with marked reactions. These were of two types: (1) In 1 case circulatory collapse was corrected by oxygen inhalations and ephedrine administration. (2) In 4 cases the level of anaesthesia was pushed too high; this complication was treated by ephedrine and pituitrin. " Metycaine " 1.5 per cent in Ringer's solution was used in all cases, the largest dose being 75 ml. and the smallest 38 ml., with an average of 65 ml. for multiparae and 95 ml. for primiparae. A 19-gauge malleable needle was used and discarded after 10 cases.

In a further series of 1,003 cases there was only 2.5 per cent of failures. Labour was induced in the great majority of cases, and in well over a half low forceps extractions were performed. Complications included a drop in blood-pressure of at least 40 mm. in 10 cases, foetal death in 1 case, maternal death in 1 case, and entry of the dural sac in 2 cases. In the event of puncture of the dural sac caudal analgesia was immediately discontinued. The maternal death was not attributable to the caudal block; the foetal death occurred in a case where the anaesthesia rose to the level of the third dorsal segment with concomitant circulatory depression and anoxia of both mother and foetus.

It is recommended that oxygen, plasma, ephedrine or " methedrine ", intravenous barbiturate, " coramine " or caffeine, and sterile spinal needles should always be immediately available. " Multiparas are injected when 3 to 4 cc. [*sic*] dilated and primiparas at 4 to 5 cc. . . . in the prone or modified knee-chest position with a pillow at the pelvis." A barbiturate may be administered first. As after 6 to 8 hours the anaesthesia diminishes and slight toxic effects are evident, it is not advisable to start anaesthesia too soon. Five to 10 minutes after giving the test dose of 8 ml. of the solution an additional 20 to 40 ml. is added and the patient is turned on her side. This will bring the level of anaesthesia to the eleventh or twelfth dorsal segment. If the level extends higher on the dependent side after a period of 10 to 15 minutes she is turned over and the procedure is continued with additional 15 to 20 ml. doses at intervals of 30 to 45 minutes as indicated by the level of anaesthesia determined by pin-prick on the abdominal wall or by return of pain. When the patient is ready for delivery the final injection is made to assure an upper level of anaesthesia at or above the umbilicus and the needle is withdrawn. Sulphathiazole ointment and a dressing are applied. In multiparae the perineum and vulva must be watched to anticipate precipitate delivery. The second stage of labour is usually terminated by forceps and episiotomy. Infection at the site of injection did not occur in any of the cases reported. Postpartum care is simplified, and patients are discharged on the eighth day.

John Challis

271. **The Management of Complications Arising from the Use of Caudal Anesthesia in Obstetrics.**

By P. E. HENDRICKS. *J. Bowman Gray Sch. Med.*, 4, 175–183, Nov. 1946. 44 refs.

272. **The Aspiration of Stomach Contents into the Lungs during Obstetric Anaesthesia.**

By C. L. MENDELSON. *Amer. J. Obstet. Gynec.*, 52, 191–205, Aug. 1946. 20 figs., 3 refs.

The incidence of aspiration of stomach contents into the lungs was 0.15 per cent in 44,016 cases of anaesthesia for obstetrics. The anaesthetic was a mixture of gas, oxygen, and ether in all instances. The aspirated material was liquid in 40 cases and solid in 5; of the latter, 3 patients (2 of whom died) had complete respiratory obstruction, while the remaining 2 had incomplete obstruction with massive atelectasis; both recovered on coughing up the obstructing material. Cyanosis, tachycardia, and dyspnoea were present, with signs of massive collapse, mediastinal shift, and consolidation. The 40 cases of aspiration of liquid material had cyanosis, tachycardia, and dyspnoea, but there was no massive atelectasis or mediastinal shift. On ausculation, wheezes, rales, and rhonchi, were heard. A pulse-rate of 160 and a respiration-rate of 40 were common. X-rays showed irregular soft mottled densities in the involved areas, but no mediastinal shift. The patients were critically ill during the acute period, but the condition became gradually stabilized within 24 to 48 hours. Films showed complete recovery in 7 to 10 days. Right lungs were more commonly involved, but massive aspiration involved both lungs. Many cases occurred before the introduction of sulphonamides and penicillin. Experimental work on rabbits bore out the results found in clinical cases. Infection is relatively infrequent, but when it does occur it is a serious complication. During labour the stomach empties very slowly, and food taken 24 to 48 hours before may be vomited. Points in prophylaxis and treatment are: (*a*) withholding oral feeding during labour; (*b*) use of local analgesia where possible; (*c*) alkalinization of and emptying of stomach contents prior to general anaesthesia; (*d*) provision of skilled anaesthetists and of adequate equipment for postural and bronchial drainage; (*e*) prompt recognition and treatment of the condition. *John Challis*

See also No. 305.

PUERPERIUM

273. **A Case of Hypophyseal Atrophy in the Puerperium.** (Un caso di insufficienza ipofisaria post-partum.)

By L. VIALE. *Arch. " E. Maragliano," Pat. Clin.*, 1, 368–376, Nov.–Dec. 1946. 30 refs.

274. **Postnatal care of the Venous System.** (Algunos aspectos sobre la revision y cuidados del sistema venoso en el postparto.)

By L. ABAD COLOMER. *Toko-ginec. Pract.*, 5, 381–391, Nov. 1946.

275. **Vaginal Malformations and the Puerperium.** (Malformaciones vaginales y estado puerperal.)

By R. GARCIA PASTOR. *Toko-ginec. Pract.*, 5, 357–370, Nov. 1946. 5 figs., 10 refs.

276. **Behaviour of Urinary Elimination of Trimethylamine in the Puerperal State.** (Comportamento dell' eliminazione urinaria di trimetilamina nello stato puerperale.)

By G. COLUCCI. *Ginecologia, Torino*, 12, 323–330, Oct. 1946. 2 figs., 15 refs.

THE INFANT

277. **Statistics of Births and Premature Births in the Foreign Paediatric Literature (1940-1945).** (Nouveau-nés et prématurés dans la littérature pédiatrique étrangère [1940-1945].)

By — SCHACHTER. *J. méd.*, Paris, 169–172, Nov. 1946. 4 refs.

278. **Hydrocephalus in a Maternity Home.** (La hidrocefalia en el Instituto de Maternidad.)

By F. URANGA IMAZ, R. DUBROVSKY, and P. ALBANESE. *Prensa méd. argent*, 33, 2038–2041, Oct. 4, 1946. 7 refs.

279. **Anoxia Neonatorum.**

By C. L. SULLIVAN. *New. Engl. J. Med.*, 235, 894–896, Dec. 19, 1946. 4 refs.

280. **Shortness of the Neck in the Newborn (Cases of Klippel-Feil Syndrome).** (I neonati senza collo. Contributo casistico sul morbo di Klippel-Feil.)

By G. VECCHIETTI. *Clin. Ostet. Ginec.*, 48, 235–245, Nov.–Dec. 1946. 6 figs., 45 refs.

281. **Notes on an Outbreak of Pemphigus Neonatorum in a Private Nursing Home.**

By G. C. WILLIAMS, C. SIMS-ROBERTS, and G. T. COOK. *Mon. Bull. Min. Health*, 6, 13–20, Jan. 1947. 10 refs.

A nursing home, well situated, with 20 beds all in large, well-ventilated, single rooms, but with only one labour ward, one sterilizing room, a small nursery, no milk kitchen, and no separation unit,

was the scene of the outbreak of pemphigus neonatorum. The bookings were limited and the average stay in the home was 14 days. The staff was adequate.

In the discussion the authors refer to a number of points of interest revealed by the investigation. Each patient had her own private practitioner in attendance and " the list of doctors was a formidable one." There was no scheme whereby the staff could be made aware of any abnormal circumstances in connexion with the different cases in the home, and each practitioner had his or her own ideas about the management of cases. General conditions in the home were excellent. Sufficient evidence was found to account for spread; for example, there was no dry-sterilization of masks and there were no facilities for drying napkins or for " dry-sweeping " the floors. Although the lesions were mild the results of swabbing showed a wide distribution of *Staphylococcus aureus* in the community. Bacteriophage typing was of great value in detecting the " epidemic strain ".

R. H. Parry

282. **Haemolytic Jaundice.** (Ictericia hemolitica.) By O. L. MARRUGAT and R. A. LAGRANDA. *Rev. med.-quirúrg. Pat. fem.*, 25, 400–410, Sept. 1946.

283. **The Feeding of Infants, with special reference to Premature Babies.** (Beitrag zur Neugeborenen-Ernährung unter spezieller Berücksichtigung der Frühgeburten.) By V. MORF. *Ann. Pædiat., Basel*, 168, 40–56, Jan. 1947. 3 figs., 10 refs.

284. **The stillbirth-rate in England and Wales in Relation to Social Influences.** By I. SUTHERLAND. *Lancet*, 2, 953–956, Dec. 28, 1946. 7 refs.

Between 1929 and 1940 the stillbirth-rate for England and Wales decreased only 5 per cent and deaths per 1,000 live births at ages under 4 weeks decreased 10 per cent, while the death-rate at ages 9 to 12 months decreased 48 per cent. The author makes a regional comparison for 1929–40; the London boroughs had the lowest and Wales (all types of area) the highest rates. Only in Scotland is a statement of the supposed cause of stillbirth required on the certificate. The return for 1943 assigned 33 per cent to difficulties in labour and accidental haemorrhage and 19 per cent to " ill-defined and unknown causes." The stillbirth-rate for a constant age is highest in nulliparae but begins to rise again after the first birth; there is a steady increase with age for all degrees of parity. As, however, there has been a considerable decrease in the stillbirth rate, especially since the war—in Wales the rate fell by 34 per cent and in England by 27 per cent between 1938 and 1944—factors of social-economic order must also be involved. During the war the environment of pregnant women deteriorated in many respects but the stillbirth-rate fell.

Two social-economic factors, however, improved —nutrition and antenatal care. A test of this explanation is to see how well the stillbirth-rate can be expressed in terms of other social-economic indices by means of a regression equation. The author used five, the crude birth-rate, the proportion of occupied males over 14 in social classes iv and v, mortality-rate of 3 to 12 months, number of persons per room in private families, and the percentage of occupied males out of work. The data related to the pre-war period. The result was, in the more favourable case (the county boroughs of England and Wales), to improve the accuracy of the estimate by about 30 per cent. [If all we know is the mean stillbirth-rate for a set of county boroughs, the best estimate we can give for each is the mean of all; but if we know the values of the five indices for each borough we should substitute a different estimate in each instance, unless, of course, the values of the indices were the same; the result would be that the square root of the average of squared deviations of predicted from observed in the second case would be about 30 per cent smaller than in the first. In other words, the indices chosen did not cover more than a moderate proportion of the factors on the stillbirth-rate].

Major Greenwood

285. **A Rare Cause of Foetal Death.** By P. P. KIRWAN. *Brit. med. J.*, 1, 297, Mar. 8, 1947. *Rh factor, erythroblastosis foetalis.*

286. **Permeability of the Human Placenta to Iso-antibodies.** By A. S. WIENER. *J. Lab. clin. Med.*, 31, 1020–1024, Sept. 1946. 15 refs.

Rh-negative individuals sensitized to the Rh factor may produce either or both of two sorts of antibodies—Rh agglutinins and Rh-blocking antibodies. The presence of Rh agglutinins can be demonstrated by direct testing in saline media, while the presence of Rh-blocking antibodies can

be demonstrated either by the so-called blocking test performed in a saline medium—that is, the demonstration that Rh-positive cells exposed to the blocking antibody became inagglutinable by agglutinating antibody—or directly by excluding crystalloids and performing the test in a protein solution. It is postulated that protein media contain a third component—"conglutinin," probably a colloidal aggregate of plasma protein. If this hypothesis is correct, Rh glutinins (blocking antibodies) must be smaller molecules than Rh agglutinins, and might then prove to pass through the placenta more readily than agglutinins.

In order to test the validity of the hypothesis the author decided to see whether the same considerations applied to immune anti-A and anti-B antibodies. Two special cases of iso-immunization to the Rh agglutinogen were investigated; both were mild cases of erythroblastosis foetalis in which there was no incompatibility between mother and foetus with regard to the Rh factor but in which the damage to the foetal erythrocytes (group A) appeared to be due to the formation by the mother (group O) of immune anti-A antibodies. Sera of mother and infant were examined and comparative titrations of anti-A and anti-B antibodies carried out in saline and serum. These showed that, whereas the anti-B titres in saline were higher in the mother's serum (8 and 64 times respectively), when titrated in serum, the anti-B reactions were equally strong in the infant's serum. This seems to show that the mothers have two kinds of antibody in their sera, and that the kind which reacts only in protein media passes through the placenta more readily. The anti-A titres in the mother's sera were equally great when tested in saline and in serum; no anti-A antibodies could be detected in the infants' sera by either technique. It is suggested that the anti-A " glutinins " in the mothers' sera constantly passed through the placenta during pregnancy in these 2 cases, and were absorbed by group substances in the group A foetus's body, thus gradually depleting the mother's body of anti-A antibodies.

P. L. Mollison

287. **Recent Developments in the Knowledge of the Rh-Hr Blood Types; Tests of Rh Sensitization.**
By A. S. WIENER. *Amer. J. clin. Path.*, **16**, 477–497, Aug. 1946. 2 figs., 73 refs.

This is a review of the author's work on the

" theory, heredity, and anthropologic applications of the Rh-Hr blood types, and also of the newer tests for Rh sensitization ". He summarizes his hypothesis that the congenital erythroblastoses comprise 3 " distinct, though related, clinical diseases ": (1) icterus gravis neonatorum, due to maternal anti-Rh agglutinins " milked " into the infant's circulation during labour; (2) congenital haemolytic disease due to " univalent Rh antibodies (Rh blockers or glutinins)" transmitted to the foetus during pregnancy; (3) icterus praecox, due to maternal alpha or beta antibodies acting on incompatible foetal red cells.

[This paper should be consulted by those interested in .Rh; that it is itself an abstract of a prodigious amount of work is indicated by reference to 47 papers written by the author and his collaborators, mostly between 1943 and 1946. The author's views on aetiology of the different forms of erythroblastosis have met with some criticism. In dealing with the " newer tests for Rh sensitization " no mention is made of the two most important recent contributions to this aspect of Rh work—Diamond's albumin test (1945) and Coombs' rabbit anti-globin test (1945).]

R. R. Race

288. **The Rh Factor as Applied to the Operation of Blood Banks.**
By L. J. UNGER, M. WEINBERG, and M. LEFKON. *Amer. J. clin. Path.*, **16**, 498–505, Aug. 1946. 1 fig., 6 refs.

The problem of choosing donors and recipients for Rh grouping is discussed, and it is concluded that the simplest and safest procedure is to group them all. During 1945, 22,631 donors to the blood bank of the New York Post-Graduate Medical School and Hospital were Rh-grouped. Of these " 14.7 per cent were Rh-negative, 1 per cent type Rh', 0.6 per cent type Rh", and 0.004 per cent type Rh'Rh"'". Anti-Rh_0 serum was used [anti-D of English workers]. Blood negative with this serum was subsequently tested with anti-Rh' [anti-C] and anti-Rh" [anti-E] sera. The rapid slide test of Diamond and Abelson (*J. Lab. clin. Med.*, 1945, **30**, 204), using oxalated whole blood and " blocking " anti-Rh_0 serum, was found to be completely satisfactory. Figures given for the results of comparative tube tests support this claim.

[The authors state that 1 in 25 Rh-negative

persons transfused with Rh-positive blood becomes sensitized. Now that more sensitive tests for immunization are available it is thought that the proportion is much higher.]   R. R. Race

289. The Rhesus Factor in Indians.

By G. W. G. BIRD. *Antiseptic*, **43**, 645–646, Oct. 1946. 2 refs.

The blood of 390 Indian soldiers, " of all religions and castes, and belonging to all parts of India ", was tested with human anti-D (anti-Rh$_0$, 85 per cent) serum; 386 subjects, or 98.9 per cent, were Rh positive. The proportion of Rh-negatives was lower than that found by other investigators who had used animal anti-Rh serum. [The results using serum of human origin should be the more reliable.]

The tests were performed in tubes, and the presence of agglutination was determined by naked-eye examination of the cell deposit. [A microscopical examination of the cell deposit, pipetted on to a slide, is more trustworthy.] " The serum was that known as anti-Rh (synonyms: anti-Rh 85 per cent, anti Rh$_0$, anti-D, etc.), i.e., it was identical with the serum which Landsteiner and Wiener first discovered in 1940 by injecting the red-blood corpuscles of Rhesus monkeys into rabbits or guinea-pigs."

[This is an error widely held. The human antiserum now called anti-Rh$_0$ or anti-D was discovered by Levine and Stetson in 1939 (*J. Amer. med. Ass.*, 1939, **113**, 126), but was, perhaps unfortunately, given no name by the discoverers. When the rabbit anti-rhesus-monkey antibody, discovered by Landsteiner and Wiener in 1940, was found to give, up to a point, the same reactions as the human serum, the antibody in the latter became known as anti-Rh.]   R. R. Race

290. Some Observations Upon the Rh Factor in Pregnancy.

By C. H. INGRAM. *Amer. J. Obstet. Gynec.*, **52**, 440–445, Sept. 1946. 12 refs.

In the obstetric service of the Western Pennsylvania Hospital during the first 15 months after routine Rh determinations and kindred studies were started, 6 cases of erythroblastosis foetalis were encountered in 1,682 deliveries—1 case per 280 deliveries. They resulted from delivery of 75

Rh-negative women (incidence of 1 in 12.5 Rh-negative women). Of 1,129 Rh determinations 10.36 per cent proved Rh-negative. Landsteiner and Wiener gave the incidence as 15 per cent among white subjects. More important probably than the inclusion in this series of a few negroes is the fact that the original work classes Rh' and Rh" as negatives while now they are classed among Rh-positive groups.

The series is small, but certain facts have been observed and impressions have been formed. These are listed in the hope that, with the experience of others, they may be helpful in the future management of Rh-negative mothers and their babies. (1) An Rh determination should be carried out on all pregnant women. In this series 4 babies have been salvaged who otherwise would have been lost. (2) A careful history of previous transfusions, as well as of pregnancies, should be taken in all Rh-negative pregnant women. If possible the donor's blood should be tested for the Rh factor before delivery. Only Rh-negative blood should be given to any Rh-negative woman who has not reached the end of her reproductive life. (3) All Rh-negative multigravidae and those who have been transfused either with Rh-positive or unknown blood should be tested for agglutinins and blocking antibodies at least once during the last 3 months of pregnancy. (4) In cases with either marked agglutination or blocking reaction preparations should be made for a full study of the infant's blood in the delivery room. If the red-cell count is 2,500,000 or less Rh-negative blood should be given by the umbilical vein before the cord is tied. (5) Whenever transfusion is indicated for the baby Rh-negative blood should be used. The author has contemplated using a suspension of washed maternal cells, but has never been forced to do so. (6) Once the cord is tied the method of administration found most useful is by a 22-gauge cannula into a surface vein, pressure being supplied by a syringe. In one case where cannula and vein had become obstructed and the baby was exhausted from transfusion efforts 75 ml. of blood was given intraperitoneally. The final result was satisfactory, though the baby displayed mild shock shortly afterwards. The author hesitated to use this routine again because of the shock. (7) Infants with erythroblastosis should not feed at the breast as breast milk contains anti-Rh agglu-

tinins. (8) Prognosis in affected babies must remain guarded in view of neurological residua such as spasticity and mental retardation attributed to kernicterus and reported by, among others, Leonard and Docter. The author's patients until the present have continued to be satisfactory. (9) The outlook for future babies appears to depend on 2 factors: first, another baby may be Rh-negative with no sign of trouble; secondly, even if it is Rh-positive it may survive with treatment. This latter outcome is more likely if pregnancy is postponed at least until the maternal blood is free from agglutinins and blocking antibodies. (10) The margin of safety is slender with full-term babies. Induction of premature labour means the added risks of prematurity. For this reason it is opposed.

[While agreeing that the intraperitoneal route is not ideal, the abstracter has also given blood on one occasion to an infant with erythroblastosis when accidents had befallen each accessible vein. The result here, too, was eminently satisfactory: cf. (a) Siperstein and Sansby (Amer. J. Dis. Child., 1923, 25, 107), and (b) Hahn et al., (J. Exp. Med., 1944, 80, 77).] *Anthony W. Purdie*

291. The Rh Types in Canadians of Japanese Race. By B. CHOWN, Y. OKAMURA, and R. F. PETERSON. *Canad. J. Res.*, 24, Sect. E, 135–143, Oct. 1946. 30 refs.

The authors collected samples of blood from 606 Japanese persons living in Canada. The samples were tested with the Rh sera anti-D, anti-C, anti-E, and anti-c. This was the first time that Japanese bloods had been so fully examined. As many of the 606 bloods were from related persons, the calculations of the gene frequencies were based on 217 samples, picked out of the larger number, believed to be from unrelated people. The following table gives the number and frequency of Rh phenotypes based on reactions with 4 antisera:

Reaction with antisera					Entire sample		Sample of unrelated individuals	
D	C	E	c	Phenotype	Number	Frequency	Number	Frequency
+	+	+	+	R_1R_2	252	0.4158	95	0.4378
+	+	−	−	R_1	205	0.3383	73	0.3364
+	+	−	+	R_1	78	0.1287	27	0.1244
+	+	−	+	R_1r	62	0.1023	20	0.0922
−	+	+	+	R''	6	0.0099	1	0.0046
+	+	+	+	R_2	2	0.0033	1	0.0046
−	−	−	+	r	1	0.0017	—	—
					606		217	

The authors' figures for the gene or chromosome frequencies were: R_1 (CDe), 58 per cent; r (cde), 7.95 per cent; R" (cdE), 2.89 per cent; R_z (CDE), 0.40 per cent; and R_2 (cDE), 30.76 per cent. It was thought that the frequencies of R_0 (cDe), R' (Cde), and R_y (CdE) were either zero or very small indeed. Comparing the observed frequency of bloods in the R_1R_2 and R_2r groups with the expected frequency, calculated from the above gene frequencies, an excess of R_1R_2 and a shortage of R_2r was disclosed. The authors consider that if their anti-C serum contained a small amount of anti-D as well, then homozygous R_2R_2 (cDE/cDE) blood may have been scored as R_1R_2.

R. R. Race

292. Inheritance of the Allelomorphs of the Rh Gene in Canadians of Japanese Race: A Study of 65 Families. By B. CHOWN, Y. OKAMURA, and R. F. PETERSON. *Canad. J. Res.*, 24, Sect. E., 144–147, Oct. 1946. 9 refs.

The results of the Rh grouping of 64 Japanese families (plus one from which the father is missing) and 176 of their children are classified according to the type of mating and the group of the offspring. The details of individual families are not given. The bloods were all tested with anti-C, anti-D, anti-E, and anti-c. This was the first time in which families other than European had been tested with these 4 anti-Rh sera. The authors conclude: "The data obtained were in agreement with R. A. Fisher's hypothesis of the allelic Rh genes. No exceptions to expected results were obtained." The sera used in the investigations were provided by Dr. Diamond and by Dr. Vogel.

[In this and the preceding paper the presentation is admirable. The authors have succeeded in making it clear when they are speaking of phenotypes and when of genotypes. They have also made clear which genotypes they expect the phenotypes in their population to include. The notation employed is the CDE of Fisher, together with the shorthand names in use in England; for example, R_1 for CDe, R_2 for cDE, r for cde.]

R. R. Race

293. The Use of Heparin when Performing Exchange Blood Transformations in Newborn Infants. By A. S. WIENER and I. B. WEXLER. *J. Lab. clin. Med.*, 31, 1016–1019, Sept. 1946. 1 fig., 10 refs.

The authors believe that the syndrome of icterus gravis neonatorum is initiated by intravascular agglutination, and that therefore the removal of Rh-positive cells and their replacement by Rh-negative cells may be expected if carried out early enough to prevent the development of the syndrome or, if given later, to arrest its development. Mathematical considerations show that if blood is injected and withdrawn at the same rate and in the same quantities the following degrees of replacement will be effected. If an amount equal to the infant's blood volume is injected there will be 63 per cent of donor's blood in its circulation at the end. If an amount equal to twice the infant's blood volume is injected the proportion of donor blood will rise to 86 per cent. The amount must be increased to 3 times the infant's blood volume to obtain a 95 per cent replacement. Since the infant at birth has a blood volume of approximately 250 ml., little will be gained by a transfusion of more than 500 ml. The following technique is recommended:

The internal saphenous vein is exposed at the ankle and a blunt 20-gauge cannula is tied into place with catgut; 0.5 ml. of heparin (500 units) is injected through the needle, and blood is then allowed to run in. An incision is made at the wrist and a short-bevel 20-gauge needle is inserted into the radial artery. This needle is not inserted until the infant has already received the first 50 ml. of the transfusion. From this point onwards the rates of transfusion and exsanguination are kept equal as nearly as possible. If any clotting occurs a further 500 units of heparin is injected. When 400 ml. of blood has been withdrawn the radial artery is tied and the skin sutured. The remainder of the 500 ml. is allowed to run in, and the whole process is thus completed.

In an actual case the authors were able to demonstrate by differential agglutination tests that the expected degree of exchange did occur, approximately 90 per cent of cells in the final arterial sample being of the same type as the donor's.

[Whether or not the authors' thesis of damage by intravascular agglutination is correct, there are good reasons for wanting to effect a temporary replacement of Rh-positive by Rh-negative cells in the infant with icterus gravis. By supplying it with Rh-negative cells, which are not susceptible

to rapid destruction, the stimulus to the bone marrow is reduced, less Rh-positive cells are produced and therefore less are destroyed. An exchange transfusion effects this process very rapidly and prevents loading of the infant's circulation with the products of blood destruction. Moreover, it must remove a large quantity of incomplete antibody from the infant's plasma. The authors' method has been found satisfactory in practice, and the only criticism is that cells in saline are injected; it would seem preferable to use heparinized whole blood for the transfusion, so as not to deplete the infant of plasma protein and so as to avoid the injection of a large amount of electrolyte, since if an ordinary bottle of stored blood is used for the transfusion the infant inevitably receives a large amount of citrate. Although the whole procedure is an attractive one, it is certainly more troublesome to perform than the ordinary drip transfusion and demands 2 to 3 hours of the operator's time. Only a large-scale follow-up of cases can show whether it brings any improvement in prognosis, particularly with regard to the late sequelae of the disease.]

P. L. Mollison

294. The Encephalopathy (Kernicterus) of Erythroblastosis Fetalis, its Serologic Diagnosis and Pathogenesis.

By A. S. WIENER and M. BRODY. *Amer. J. ment. Defic.*, **51**, 1–14, July 1946. 3 figs., 34 refs.

A new theory is advanced to explain the occurrence of neurological signs and symptoms in jaundiced infants suffering from erythroblastosis foetalis. The condition, named kernicterus by Schmorl in 1903, is the result of areas of degeneration of ganglion cells, associated with demyelination, disseminated throughout the brain, usually but not necessarily revealed to the naked eye by bile-staining. The actual neurological picture depends on the extent and distribution of these areas, and may be extremely variable. It is claimed that the cerebral damage is the result of the formation of agglutination thrombi in capillaries of the brain, and that these are readily demonstrable in haematoxylin and eosin sections. Diamond, Blackfan, and Baty in 1932 demonstrated that congenital haemolytic anaemia, icterus gravis neonatorum, hydrops foetalis, and certain stillbirths all have a similar pathology, and suggested that

they are due to a common disease process. The discovery of the Rh factor by Landsteiner and Wiener in 1940 was soon followed by Levine's observations on iso-immunization in pregnancy and his theory of the causation of erythroblastosis. According to this theory, " an Rh-negative mother bearing an Rh-positive foetus may become sensitized to the Rh factor, and the Rh agglutinins thus produced may pass back through the placenta into the foetus, causing destruction of the blood of the foetus and giving rise to one or another manifestation of erythroblastosis ". A drawback to this hypothesis is that such agglutinins are demonstrable in less than half the proven cases of Rh-sensitivity, and no attempt is made to explain the variable clinical manifestations of erythroblastosis in different infants. About 10 per cent of all marriages involve Rh-negative women with Rh-positive husbands and children, yet only one in approximately 300 newborn infants is affected by erythroblastosis, presumably because only occasional Rh-negative women are readily sensitized to the Rh factor. Erythroblastosis can occur when the mother is Rh-positive, though the Rh factor accounts for 90 per cent of all cases. The other most common cause appears to be iso-immunization to the ordinary A-B blood group factors, although occasionally cases are shown to be due to variants of the Rh factor. The presence of sensitivity must be demonstrated by showing that abnormal antibodies (usually anti-Rh) are present in the mother's serum, as the mere demonstration that the mother is Rh-negative and the infant Rh-positive does not necessarily or usually indicate sensitivity.

A new type of antibody which does not produce agglutination of sensitized red cells was demonstrated in 1944 by Race and Wiener. These so-called blocking antibodies or glutinins are presumed to be univalent and to consist of smaller molecules than Rh agglutinins, which are probably bivalent in the chemical sense that each molecule has two specific combining groups for the corresponding antigen, and hence clumping of red cells takes place by the formation of a lattice-work. Blocking antibodies are able to combine with red cells in saline without producing any visible reaction, though in serum or plasma they can bring about clumping (conglutination) by the adsorption of X protein (conglutinin).

The authors believe that most of the cases of erythroblastosis complicated by neurological sequelae are due to the presence of agglutinins (bivalent antibodies) in the mother's serum, transferred to the foetal circulation during parturition, when the uterine activity "milks" them through the placenta. Because of their large molecular size these antibodies are not likely to traverse the placenta during pregnancy, and it is commonly found that these infants appear normal at birth, but soon become jaundiced and show signs of toxicity. The action of these antibodies is to cause agglutination of the infant's red cells in vessels where the circulation is slow, producing agglutination thrombi. The severe jaundice is the result of liver damage consequent on this pathological process, and involvement of bone marrow causes release of erythroblasts, often without any anaemia. Kernicterus is due to the same process in the brain. Occasionally the theory appears to break down by the occurrence of cases with only univalent Rh antibodies in the mother's serum, but it is believed that the development of X protein in the infant's serum (by dehydration or other mechanism) results in conglutination of the infant's red cells with sequelae indistinguishable from those of agglutination. Early and massive transference of univalent antibodies, which more readily traverse the placenta, results in a hydropic stillbirth because of the breakdown of " coated " red cells producing severe anaemia without agglutination. In milder cases the infant is born alive and can be saved by proper transfusion therapy with Rh-positive blood or the mother's washed red cells. This variety is ordinarily not complicated by kernicterus, but mixed pictures can occur due to the presence of both univalent and bivalent antibodies.

Alpha or beta antibodies developed in the maternal serum in response to A and B agglutinogens in the red cells of infants of an incompatible blood group may occasionally result in breakdown of their red cells and mild jaundice, often classified as physiological icterus. Occasionally severe or fatal instances of erythroblastosis may result from this mechanism, but this is exceptional because the placenta is relatively impermeable to natural alpha and beta agglutinins and the agglutinogens A and B are not well developed in infants' red cells.

Illustrative case histories with the results of serological examinations are described, one being a severe case of erythroblastosis due to sensitization to agglutinogen B, resulting in bilateral optic atrophy and complete idiocy. Pneumoencephalography revealed severe and widespread cerebral atrophy. It is emphasized that iso-immunization has not been demonstrated in Wilson's disease (3 cases) and that there is no relation between this condition and erythroblastosis. Early clamping of the umbilical cord is suggested to limit the transference of agglutinins from mother to child.

M. Baber

295. **The Rh Factor and its Importance in Medical Practice.** (Il fattore Rh e la sua importanza nella prassi medica.)
By F. DOMENICI. *Gazz. sanit. Milano.*, 17, 137–140, Nov.–Dec. 1946.

296. **Role of the Rh Factor in Erythroblastosis.** (Rôle du facteur Rh dans l'érythroblastose du nouveau-né.)
By A. BERTRAND. *Union méd. Can.*, 75, 1384–1390, Nov. 1946. 11 refs.

297. **Variation in the Titre of Rh Antibody during Pregnancy.**
By M. D. HICKEY and E. DE VALERA. *Brit. med. J.*, 1, 335, March 15, 1947. 3 refs.

298. **The Rh Factor in Obstetrics.**
By E. JOOSTE. *S. Afr. med. J.*, 20, 732–739, Dec. 14, 1946. 18 refs.

299. **The Rh Factor and Foetal Erythroblastosis.** (Factor Rh e eritoblastoses fetaes.)
By V. MONETTI. *Rev. Ginec. Obstet.*, 2, 154–163, Sept. 1946. 24 refs.

300. **The Rh Factor and Erythroblastosis.**
By C. E. SNELLING. *Canad. med. Ass. J.*, 56, 47–51, Jan. 1947. 28 refs.

301. **Mild Cases of Erythroblastosis Foetalis.** (Lichte gevallen van erythroblastosis foetalis.)
By S. I. de VRIES. *Ned. Tijdschr. Geneesk.*, 91, 13–20, Jan. 4, 1947.

OBSTETRIC OPERATIONS

302. **Episiotomy.** (L'épisiotomie.)
By F. CHATILLON. *Rev. méd. Suisse rom.*, 66, 777–782, Nov. 25, 1946.

303. **The Lower Segment Caesarean Operation.**
By J. RIDDELL. *Med. Pr.*, 217, 71–75, Jan. 22, 1947. 3 figs.

304. **Advisability of Caesarean Section.** (Oportunidad de la cesárea vaginal.)
By R. RAMIREZ MERCHAN. *Med. Cirug.*, 10, 433–436, Sept. 1946.

305. **Local Anesthesia for Cesarean Section.**
By F. P. LIGHT. *N. Y. St. J. Med.*, 47, 48–52, Jan. 1, 1947. 3 figs., 1 ref.

GYNAECOLOGY

General

306. **Gynaecology in 1946.** (La gynécologie en 1946.)
By R. PALMER, *Paris méd.*, 36, 561–564, Dec. 21, 1946.

307. **Essentials to Adequate Gynecologic Patient Study.**
By A. L. DIPPEL. *Tex. St. J. Med.*, 42, 417–422, Nov. 1946.

308. **Frigidity: Aphrodisiac Effect of Testosterone Implantations.** (La frigidité; effets aphrodisiaques des implantations de testostérone.)
By I. BERNARD. *Gynécologie*, 43, 201–209, Nov.–Dec. 1946.

Disorders of function

309. **Menstrual Insufficiency and its Treatment.** (Insuffisances menstruelles et leur traitement.)
By F. MORICARD. *Rev. franç. Gynéc.*, 42, 20–28, Jan. 1947.

310. **Functional Dysmenorrhoea. Physiopathological Conception.** (Les dysménorrhées fonctionnelles. Conceptions physiopathologiques.)
By A. E. LIESSE. *Rev. franç. Gynéc.*, 42, 29–38, Jan. 1947. 22 refs.

311. **The Climacteric—A Period of Endocrine Imbalance.**
By J. H. DARRAGH. *McGill med. J.*, 15, 239–249, Oct. 1946. 12 refs.

312. **A Contribution to the Diagnosis of the Menopause.** (Een bijdrage tot de diagnostiek van het climacterium.)
By L. H. LEVIE. *Ned. Tijdschr. Geneesk.*, 91, 204–206, Jan. 25, 1947.

313. **Value of Irradiation of the Pituitary Glands in Menopausal Disorders.** (Uber den Wert der Hypophysenbestrahlung bei klimakterischen Ausfallserscheinungen.)
By A. KOTEK. *Wien. klin. Wschr.*, 58, 714–716, Nov. 29, 1946. 7 refs.

The results of irradiation of the pituitary gland

in 200 cases of menopausal disorder have been observed by the author over a period of at least 3 years at the Second University Clinic for Women's Diseases, Vienna. The disorders were mostly nervous, without evident anatomical lesions, 'and were partly due to an increase in adrenaline secretion (Högler test); hot flushes and palpitations were the most frequent complaints. The author found that all 200 patients complained of hot flushes, 102 of excessive sweating, about 60 of headache and dizziness and 3 of joint pains. Out of the 200, 25 had had a physiological menopause, 117 had been sterilized by X-rays, and 9 sterilized by operation; the remaining 49 had had a radical operation for carcinoma and prophylactic application of X-rays. No essential connexion was found between the origin of the menopause and the subsequent disorders. In treatment two exposures were given to the temporal region, a little above the middle of a line joining the lateral orbital margin with the external auditory meatus. The exposed fields had a diameter of 4 cm. Each dose measured 200 r at 180 kV. and 6 mA., at a skin distance of 30 cm., and with a filter of 0.4 mm. copper and 1 mm. aluminium. Steinhardt and a few others have recommended 4 to 5 applications, but recently, owing to the danger of skin lesions, attempts to obtain better results with more than 2 exposures have been abandoned.

Results of treatment were classified under 3 headings: (1) age of patient; (2) original cause of the menopausal disorder; (3) time elapsed before beginning irradiation.

TABLE I

	Total number of patients	Patients under 40 years	Patients aged 41–45 years	Patients aged 46–50 years	Patients over 50 years of age
Cured ..	21	4 (11%)	6 (10%)	6 (8%)	5 (14%)
Improved	104	17 (48%)	31 (54%)	38 (51%)	18 (53%)
Not improved	75	14 (41%)	20 (36%)	30 (41%)	11 (33%)

Table I shows no connexion between results and any specific age. Four women under 40, all patients who had been treated by the radical operation for carcinoma of the cervix and later given X-ray therapy, showed the best results from X-ray treatment of the pituitary. This finding was general among patients who had received such treatment for carcinoma as is shown in Table II.

TABLE II

	Physiological Menopause	Surgical Sterilization	X-ray Sterilization	Carcinomata	Total
Cured ..	—	—.	14 (12%)	7 (14%)	21 (10.5%)
Improved	13 (52%)	5 (55%)	61 (52%)	25 (51%)	104 (52%)
Not improved	12 (48%)	4 (45%)	42 (36%)	17 (35%)	75 (37.5%)

Better results were obtained when the lower abdomen had been irradiated, as in X-ray sterilization or post-operative irradiation given for carcinoma. This observation has also been made by Steinhardt, but no explanation of it is known. There was no essential difference in the percentage results when classified by lapse of time since the menopause. Among the 200 cases were 6 women who reported no improvement after pituitary irradiation, but spontaneous improvement 2 to 7 years later.

Summarizing the results, the author states that 10.5 per cent of 200 patients were permanently cured; this contrasts with the figures of Borak, Porchownik, and Steinhardt, which were much higher. In the 104 (52 per cent) patients who showed improvement, 50 have been irradiated 2 or 3 times at intervals of 2 to 15 months, owing to recurrence of their symptoms. If after 3 periods only slight improvement had taken place no further irradiation was given, in view of the danger of local skin lesions. After the second irradiation an interval of 6 to 12 months had to be allowed. The improvement lasted twice as long after the second irradiation as after the first; this excludes a psychological factor. Considering that 75 in 200 cases (37.5 per cent) were absolute failures, this treatment can scarcely be recommended and has been discontinued at the Vienna University Clinic.

M. Schieber

314. **The Treatment of Benign Menopausal Bleeding.**
By J. R. WILLSON. *J. Kansas med. Soc.,* 47, 493–495, Nov. 1946. 3 refs.

315. **Treatment of Leucorrhoea.** (Tratamiento del flujo genital.)
By A. A. PUNTEL and E. A. PIZARRO. *Rev. Med. Cien. af.,* 8, 886–893, Nov. 1946.

316. **Sterility.** (Stérilité.)
By F. X. DEMERS. *Union méd. Can.,* 75, 1462–1468, Nov. 1946.

I

317. The Decline in Fertility.
By P. H. J. Turton. *Med. Offr.*, **76**, 249–250, Dec. 7, 1946.

The author deals with the social consequences of a decline in fertility. For more than 60 years the birth-rate of England and Wales has declined while the population has increased. During this period there was a rise of 68 per cent in those aged 65 years and over, and a decrease of 14.4 per cent in those under 25. In the future, simultaneously with the raising of the school-leaving age to 16 years and the maintenance of conscription, the number of old-age pensioners will go up steadily to a figure representing 31 per cent of the total population in 1961, so that it will be difficult to find the workers to carry this load of passengers. A chart gives the age distribution of population for England and Wales. The author, quoting extensively from the criticism of Joad and Desmond MacCarthy by Harrod in the *Economic Journal*, states that " . . . unless a rather spectacular increase in the size of families occurs in the decades immediately ahead, the decline of population will not be arrested in the twentieth century. . . . Those who wish to arrest the decline are charged with seeking cannon fodder. . . . In Britain such an argument, whatever truth it may have had in the past, is now obsolete."

Discussing the problems of the aged, the author remarks that the aged and infirm cannot be discarded as so much worn-out junk fit only for the scrapheap. An increase in number of hospital beds for the senile and chronic sick is useless without additional staff. Not only is the problem of the chronic sick not being met, but most people do not realise that there is a problem. The present insufficient accommodation is often in grim, depressing, ill-cared-for institutions. As by 1950 there will be over 5,000,000 people over 65 years of age, the need for more and better beds for old people is urgent. The author ends his critical survey by expressing the opinion that many trained personnel are being wasted. Industrial firms engage the services of registered nurses to act as dressers and attendants in first-aid rooms; to a large extent the services of these could be more usefully employed where the need is more urgent. [Many would consider it more important for a nation to maintain the health of the active worker than to relieve the old and infirm.]   *A. Michael Critchley.*

318. A Case of Sterility.
By E. Jacobson. *Psychoanal. Quart.*, **25**, 330–350, July 1946. 5 refs.

The case of a married woman of 35 is described. She had started to menstruate at 14 and up to 16 had developed rapidly and menstruated very freely. She worried about her obesity, dieted, worked too hard, lost weight rapidly, and became amenorrhoeic. She was so markedly of the glandular dysfunction type that her condition was diagnosed as Simmonds's disease. She married at 24 in spite of her amenorrhoea. She improved on oestrin and menstruated a few times, but did not become pregnant. She adopted a child, but this was not a success, and it was only when she came for analytical treatment that she began to improve. She gained weight and after 6 months desired to adopt another child, but in the eighth month of treatment became pregnant and was delivered of a healthy girl. Although analysis was not complete the patient was so happy that she broke off treatment, though she returned later for intermittent help. She came of a poverty-stricken Jewish family with a gentle father and very domineering mother. In prepuberty she had gone through a phase of over-submissiveness and then one of extreme aggression. This was followed by a stormy love affair with a Gentile boy, which filled her with deep guilt feelings; later she married a Jew. Dreams illustrative of her strong ambivalent feelings towards her parents and siblings are narrated. In this case there was violent regression to pre-genital oral and anal levels with some constitutional factors. The feature of the case is the amazing glandular changes which were apparently psychically determined and the extraordinary change induced by analysis. She became pregnant twice more but underwent abortions. For a time she wished to submit to artificial sterilization; although she abandoned this project she again became amenorrhoeic, which made her very happy and solved her problems. As the author remarks, the neurosis had the last word.   *R. G. Gordon*

319. A Review of the Present Position of the Investigation of Sterility and Infertility in the Female.
By C. B. Murless. *S. Afr. med. J.*, **20**, 788–793, Dec. 28, 1946. 13 refs.

320. Evaluation of the Male Factor in Conjugal Sterility. (Evaluation du facteur masculin dans la stérilité conjugale.)

By R. Palmer and G. Guillon. *Rev. franç. Gynéc.*, 42, 1–19, Jan. 1947. 23 figs., 14 refs.

Abnormalities of the reproductive organs

321. A Case of Pseudohermaphroditism Treated by Surgery and Hormones. (Un cas de pseudohermaphrodisme, traité par la voie chiruogicale et hormonale.)

By M. R. Tachezy. *Scapel. Brux.*, 99, 722–725, Nov. 30, 1946. 9 figs.

322. Vulvar and Vaginal Dystrophy: Kraurosis Vulvae. (De la dystrophie vulvaire et vaginal dite " Kraurosis vulvae ".)

By P. Moulonguet. *Paris méd.*, 36, 564–567. Dec. 21, 1946.

323. Severe Cases of Stenosis of the Female Urethra. (Uber hochgradige Stenosen der weiblichen Urethra.)

By G. Tzamaloukas. *Klin. med., Wien.*, 1, 553–556, Nov. 1, 1946. 17 refs.

324. Uretero-vaginal Fistula. (A propos de fistule urétéro-vaginale.)

By P. Bourgeois and R. Simard. *Union méd. Can.*, 75, 1645–1647. Dec. 1946.

Infections of the reproductive organs

325. The Importance of the pH in the Treatment of Diseases of the Vagina.

By C. A. Anderson. *North Carolina med. J.*, 8, 29–31, Jan. 1947. 1 ref.

326. Results Obtained with Penicillin Treatment of Gonorrhoea. (Ergebnis der Tripperbehandlung mit Penicillin.)

By K. Hoede, E. Bayer, and K. D. Ebbinghaus. *Med. Klinik.*, 41, 443–446, Oct. 1946. 1 ref.

New growths of the reproductive organs.

327. Epithelial Changes in the Uterine Glands in Glandular-Cystic Hyperplasia. (Uber eigentümliche Epithelveränderungen an den Uterindrüsen bei glandulärzystischer Hyperplasie.)

By I. Obiditsch-Mayer. *Klin. Med., Wien.*, 1, 500–505, Oct. 1, 1946. 4 figs., 10 refs.

The author found some large cells, which he likens to Hamperl's " onkocytes ", in the glands of a hyperplastic endometrium. [The grounds for such a comparison are dubious, even if one accepts Hamperl's ideas about " onkocytes ".]

R. A. Willis

328. Tumours of the Female Genital Tract.

By R. W. Te Linde. *Bull. N. Y. Acad. Med.*, 23, 10–19, Jan. 1947.

329. A Cancer Control Project in a Planned Parenthood Center.

By E. V. Berg. *Hum. Fertil.*, 2, 75–78, Sept. 1946.

The author's work was inspired by a report by MacFarlane and others which appeared in January 1942, in the *Pennsylvania Medical Journal*. This report described an attempt to control cancer of the uterus by pelvic examination twice a year of volunteers, ranging in age from 30 to 80. In the first 1,000 individuals examined, 4 cases of cancer were found and 471 benign lesions, of which 291 were considered to be " precancerous lesions of the cervix ". The author describes a similar scheme applied to women attending the Nassau-Suffolk Planned Parenthood Center and the findings in the first 1,000 patients. They were all married women. No case of cancer was discovered, but 525 of the patients had local disease which justified reference to their own physician. The lesions discovered are analysed in a table. Only 39 of the 525 had had previous treatment or were at the time under treatment for these conditions. A further 319 received treatment after their first visit to the Center, and a table is included of the types of treatment carried out. [It would be interesting to know what happened to 167 of the 525, for it is not recorded that they received treatment.] The advantages of the scheme in relation to such a centre are discussed. *R. H. Parry*

330. Vaginal Cell Examination as a Routine in Diagnosis. A Study of Vaginal and Cervical Cytology as Related to Abnormal Growths.

By J. E. Ayre. *Sth. med. J.*, 39, 847–852, Nov. 1946. 6 figs., 13 refs.

Cytological studies were made on 2,320 patients for the diagnosis of gynaecological cancer; 226 reports were " positive ", and of these 202 were confirmed by biopsy. The error rate of a negative diagnosis proved to be 4.8 per cent, and of a positive one 1.13 per cent. The author has followed on the pioneer work of Papanicolaou, but has altered the latter's technique by taking suction specimens of the squamo-columnar junction of the cervical canal. The underlying principle of the study is that the epithelium derived from the Müllerian tract possesses the characteristic of desquamation, and that the cells so thrown off pass in the physiological stream down the uterus, tubes, and vagina. Most malignant lesions here are exfoliative, and hence they too tend to desquamate.

Besides the provision of easy and rapid diagnosis of evident cancer the author is convinced that this technique will be of great help in diagnosing cases in a clinically " pre-cancerous " condition, and thus enable operation or other treatment to be carried out much earlier.

The signs considered diagnostic of a pre-cancerous condition are the presence of anaplastic squamous cells, an abnormally high degree of cornification in the cells, multinucleation of these cells, and the finding of atypical cornified cells with dense pyknotic nuclei. In the series 19 such cases were identified. These conformed to Novak's description of the pre-cancerous state as lesions which exhibit cell activity unusual in benign conditions and yet lack certain characteristics of actual cancer. An easy method of carrying out this form of biopsy and keeping the specimens fresh for postal transmission is described. The smear is fixed in ether and alcohol for an hour, and then a small quantity of glycerin is put on it and the slide is covered by another. The individuals diagnosed as pre-cancerous were also submitted to investigations of thiamine and oestrogen activity; they showed high endogenous oestrogen levels with a thiamine deficiency. Similar changes were observed in 50 cases of proved cancer, but not in 50 control cases of benign lesions. The possibility of the existence of a metabolic factor in uterine cancer is therefore raised. The smear technique has obviously also application to most conditions in the genital tract.

Kenneth Bowes

331. Haemoperitoneum due to Ectopic Chorion-epithelioma. (Emoperitoneo da corioepitelioma ectopico.)
By F. MATTEACE. *Clin. oster. ginec.*, 48, 180–191, Sept.–Oct. 1946. 19 refs.

The author records a case in which death from haemoperitoneum occurred 18 months after the expulsion of a vesicular mole. There had been two negative laparotomies. The Friedmann reaction had been weakly positive throughout. Only at necropsy was the diagnosis made of chorion-epithelioma arising retroperitoneally near the bifurcation of the common iliac artery. The author reviews the literature and discusses the pathology and clinical features, concluding that many cases of chorionepithelioma are, like the one described, difficult to diagnose.   *A. S. Bullough*

332. Recurring Hematocolpometra Associated with Carcinoma Treated by Partial Hysterectomy: Report of Case.
By L. C. HALLENDORF and W. R. LOVELACE. *Proc. Mayo Clin.*, 22, 38–40, Jan. 22, 1947. 4 refs.

333. Solid Tumour of the Vulva. (Tumor solido da vulva.)
By A. R. de OLIVEIRA MOTTA. *Rev. Ginec. Obstet.*, 2, 273–277, Nov. 1946. 3 figs.

334. Twenty Cases of Carcinoma of the Cervix Uteri Treated by Radiosurgery. (Gosset-Wallon Technique.) (Une série de vingt cancers du col utérin traités par l'association radium-chirurgie [technique de Gosset-Wallon].)
By J. LANGE. *Bordeaux. chir.*, 14–20, Jan.–Apr., 1947.

335. Rhabdomyosarcoma of the Cervix and Vagina in a 7 months old Infant. (Uber ein rhabdomyomatöses Traubensarkom der Cervix und Vagina bei einem 7 Monate alten Kind.)
By W. KOHLMEIER. *Klin. Med.*, 1, 571–577, Dec. 1, 1946. 3 figs., 6 refs.

336. Fibromyoma of the Uterine Cervix. (Contribution à l'étude du fibromyome du col utérin.)
By —. BOURG and —. HANNES. *Brux. méd.*, 27, 577–583, Mar. 16, 1947. 1 fig., 25 refs.

337. Endophytic Carcinoma of the Cervix Uteri with " Portio Lacunaris ". (Ein endophytisches Kollumkarzinom mit einer " Portio lacunaris ".)
By V. GRUNBERGER. *Krebsarzt*, 1, 522–528, Dec. 1946. 3 figs., 5 refs.

338. Metastasis of Carcinoma of the Cervix Uteri Adnexa. (Zur Kenntnis der Metastasierung des Kollumkarzinoms in die Adnexa.)
By O. SCHINKELE. *Klin. med.*, 1, 595–601, Dec. 1, 1946. 4 figs., 13 refs.

339. Cervical Stump Carcinoma after Subtotal Hysterectomy. (Cancérisation du moignon du col utérin après hystérectomie subtotale.)
By G. SAINT-ARNAUD. *Laval méd.*, 11, 906–910, Nov. 1946. 7 refs.

340. Calcareous Tumours of the Uterus. (Tumores calcareos uterinos.)
By E. St. LOOP. *Obstet. Ginec. lat.-amer.*, 4, 836–841, Nov. 1946. 2 figs., 5 refs.

341. Independent Treatment of a Malignant Tumour of the Uterus in Labour. (Przypadek samoistnego wyleczenia zamartwiczego miesniaka maccicy w pologu.)
By J. DOLINSKY. *Polsk. Tyg. lek.*, 1, 1125–1127, Sept. 16, 1946.

342. A Case of Combined Subserous Pedunculated Fibroma and Sarcoma of the Uterus. (Su di un caso di associazione neoplastica dell'aparato genitale feminile.

[Fibroma peduncolato sottosieroso e leiosarcoma dell' utero].)

By L. de BELLIS. *Clin. Ostet. Ginec.*, 48, 246–253, Nov.–Dec. 1946. 2 figs., 17 refs.

343. A Case of Endometriosis Ilei. (Et Tilfaelde af Endometriose i Ileum.)

By T. POULSEN. *Nord. Med.*, 33, 63–64, Jan. 10, 1947. 1 fig., 3 refs.

344. Adenomyosis of the Uterus. A study of 52 Reported Cases and a Review of the Literature.

By S. D. SPATT. *Amer. J. Obstet. Gynec.*, 52, 581–587, Oct. 1946. 39 refs.

The author presents 52 cases of uterine adenomyosis in which the endometrium has been carefully studied. He correlates his findings with those of others in a review of the literature. Endometrial findings are probably of the greatest value at the present time in the study of abnormalities of ovarian secretion, owing to the difficulty of obtaining accurate direct hormone titres. Varying figures are given by different authors for the incidence of adenomyosis, but it is concluded that it occurs in 5 to 10 per cent of myomatous uteri. The highest number of cases occur between the ages of 40 and 50. Symptoms in the present series were " metromenorrhagia " in 56 per cent, dysmenorrhoea in 29 per cent, both together in 17 per cent, and backache in 3 per cent, but in no case was adenomyosis present alone. The endometrium was studied in 50 out of the 52 cases and the anovulatory cycle was found to be present in 31. It is suggested that over-production of oestrogen may be a common factor in causing the endometrial changes and the adenomyosis. Fibroids and adenomyosis are also frequently associated, suggesting a common aetiology. Pelvic inflammation and ovarian cysts were also frequently found.   *Josephine Barnes*

345. Angiomyomatosis of Uterus. (Angiomyomatose de l'utérus.)

By J. P. DAVEO and J. MORISSON-LACOMBE. *Rev. franç. Gynéc.*, 41, 352–355, Nov. 1946. 1 fig., 4 refs.

346 Dysgerminoma of the Ovary.

By W. C. CUSTER. *Surgery*, 20, 520–524, Oct. 1946. 3 figs., 4 refs.

Dysgerminoma of the ovary arises from undifferentiated sex cells of the primitive mesenchyme and tends to occur in young subjects whose secondary sex characteristics may be abnormal. Its incidence among malignant ovarian tumours is variously

given as between 3 and 6 per cent. The presenting symptom in these cases is usually abdominal distension, pain and menstrual irregularities being rare. Sex hormone studies are of no value in diagnosis, which is usually made at operation. The tumour must always be regarded as malignant and treated by operative removal. X-ray irradiation is without effect.

A case is reported in a 12-year-old girl in whom the presence of an abdominal mass had been found at a routine examination. The mass extended from the left side of the pelvis to above the umbilicus, was irregular and mobile and not tender on palpation. Pelvic examination did not allow of its differentiation from the uterus. Laparotomy disclosed a large mass, weighing over a kilogramme and replacing the left ovary, firm, discrete, and non-adherent to surrounding structures. The surface was opaque, pale grey, and fairly smooth. On section, patches of haemorrhage and degeneration were seen, but no cystic areas. Histologically, the tumour consisted of cords and nests of large cells with pale cytoplasm and large vesicular nuclei, often with atypical mitotic figures, and with a variable amount of fibrous stroma.

A follow-up examination of the child 18 months later revealed no evidence of recurrence or metastasis.   *S. S. B. Gilder*

347. Gonocytoma. Homologous Ovarian and Testicular Tumours. I. With Discussion of " Mesonephroma Ovarii." [In English.]

By G. TEILUM. *Acta path. microbiol. scand.*, 23, 242–251. 1946. 13 figs., 14 refs.

The author applies the term " gonocytoma " to a series of similar tumours which occur in the ovary and the testis. In the testis the tumours derive from early stages of the germ cells, and in the ovary from the homologous cells in the remnants of the medullary cords. The normal disappearance of these cells from the ovary explains the lower frequency of the tumours in women, their restriction to lower age groups, and the frequent coexistence of developmental abnormalities of the genital organs. Three subdivisions are recognised in testis and ovary. Gonocytoma I corresponds with seminoma in the testis and with dysgerminoma in the ovary; it does not produce chorionic gonadotrophin. Gonocytoma III corresponds with chorionepithelioma in both testis and ovary and

secretes chorionic gonadotrophin. Gonocytoma II, with which this paper is particularly concerned, is an " intermediate form ", both histologically, and in the irregular secretion of gonadotrophin.

Teilum describes 4 malignant, radio-resistant tumours of the testis in men ranging from 26 to 40 years of age. Histologically the tumours were most often adenopapilliferous; they were either solid or cystic and sometimes teratoid, and transitions were traced on the one hand to undifferentiated seminoma and on the other to chorionepithelioma. He makes a detailed comparison of these tumours with ovarian tumours variously described and called mesonephroma ovarii by Schiller (*Amer. J. Cancer*, 1939, 35, 1), and concludes that the testicular and ovarian tumours are similar in structure and origin, both belonging to the " intermediate form ", Gonocytoma II. He contrasts with Schiller's tumours a malignant ovarian tumour in a woman aged 45; this tumour he considers to be a true mesonephroma. *L. Foulds.*

348. Arrhenoblastoma—Androblastoma. Homo-logous Ovarian and Testicular Tumours. II. Including the so-called " Luteomas " and " Adrenal Tumours " of the Ovary and the Interstitial Cell Tumours of the Testis. [In English.]
By G. TEILUM. *Acta path. microbiol. scand.*, 23, 252–263, 1946, 23 figs., 30 refs.

In addition to the gonocyctoma (see Abstract No. 347) the author recognises a second series of homologous tumours occurring in both ovary and testis—namely, the arrhenoblastoma or andro-blastoma series. Robert Meyer derived the arrhenoblastoma of the ovary from testicular elements remaining from early stages of gonado-genesis. On this hypothesis similar tumours would be expected in the testis, but none has been described hitherto. Teilum now describes such a testicular tumour removed from a man aged 53. The left testis had been enlarged for 30 years, but had increased in size during the last 2 years; impotence had been present for 3 years, and gynae-comastia for 1 year. The gynaecomastia subsided partially after removal of the enlarged tesis. The histological picture was very varied, but transitional forms showed that the diverse structures repre-sented different stages of differentiation of a single blastoma. All the characteristic histological features of ovarian arrhenoblastoma were present. Further, gradual transitions were demonstrated

from tumour tissue of androblastoma type to clear-cut " lipoid cell tumour ". This tissue was histologically identical with that of the lipoid-containing ovarian tumours which, though usually described as " luteoma ", " adrenal tumour ", " ovarian hypernephroma ", or " folliculome lipidique ", should now be regarded as particularly lipoidal forms of ovarian arrhenoblastoma. Other variants show a more or less pronounced differen-tiation in the direction of testicular interstitial-cell tumour and a homologous " extra-glandular " interstitial-cell tumour of the ovary. The andro-blastoma (arrhenoblastoma) series represents a later developmental stage than the gonocytoma and shows differentiation in greater or less degree towards normal testicular elements. The fact that the tumours are virilizing in women and femin-izing in men does not, in Teilum's opinion, dis-prove their homology, for this paradoxical effect is commonly shown by adrenal tumours; prob-ably chemically related steroid substances with oestrogenic or androgenic activity are present in addition to the normal sex hormones.

L. Foulds

349. Gangrenous Ovarian Cyst in a Child of Four, and Rupture of the Heart.
By E. R. SELBY. *Canad. med. Ass. J.*, 56, 74–75, Jan. 1947.

350. A Case of Psammocarcinoma of the Ovaries Developing After 18 Years. (Un cas de psammo-car-cinome des ovaires qui évolue depuis 18 ans.)
By R. SARASIN. *Gastroenterologia, Basel*, 71, 315–321, 1946. 3 figs.

351. Cystic Teratoma of the Ovary Infected with *Eibethella typhi*. (Teratoma quistico del ovario, infectado por bacilos de Eberth.)
By A. DURAN BUENDIA and S. FUENZALIDA. *Bol. Soc. chil. Obstet. Ginec.*, 11, 141–143, Sept. 1946.

352. Tumours of the Ovarian Parenchyma. (Les tumeurs du parenchyme ovarien.)
By A. CORNIL. *Acta chir. belge.*, 45, 363–394, Dec. 1946. 7 figs., bibliography.

353. Co-existent Primary Carcinoma of the Fal-lopian Tube and of the Breast. Report of a Case.
By J. F. CURRAN and E. A. KILROY. *New. Engl. J. Med.*, 236, 64–65, Jan. 9, 1947. 4 refs.

Operations
354. Observations on Hysterectomy.
By J. K. FEENEY. *Irish J. med. Sci.*, 6th series, 1–13, Jan. 1947.

This is a detailed review of 508 hysterectomies (3 Wertheim, 275 abdominal total, 105 abdominal sub-total, and 125 vaginal) performed by the author and Prof. J. F. Cunningham in St. Vincent's Hospital, Dublin, and in nursing-homes. It covers in detail the various indications for and the advantages and disadvantages of the 4 types of operation. The overall mortality rate was 0.59 per cent. Major accidents, complications, and post-operative morbidity are discussed. Of 19 patients with carcinoma of the body of the uterus 18 were treated by abdominal total hysterectomy and 1 (with procidentia) by vaginal hysterectomy. Two are alive and well after 5 years, 4 after 3 years, 3 after 2 years, 1 after 18 months, and 1 after 6 months. Eight died of a recurrence of the growth within periods varying from 4 to 16 months. There was 1 death in operation.

A considerable part of the paper is devoted to a description of pre-operative preparation for abdominal hysterectomy and the technique of the operation of abdominal total hysterectomy. On 40 occasions vaginal hysterectomy was performed under local analgesia, using 1 per cent " novutox " after morphine-scopolamine sedation. There are no references.

[The technique of local infiltration for vaginal hysterectomy is not discussed. There is no indication whether the operators have abandoned this method of analgesia (40 out of 125 cases) or not. No mention is made of inversion of the vagina following abdominal total hysterectomy. As the operators do not stitch the round-ligament stumps to the vaginal angles, it would have been interesting to record whether inversion occurred or not.]

G. Gordon Lennon

'355. A Report of 2,798 Vaginal Hysterectomies. By Z. B. CAMPBELL. *Amer. J. Obstet. Gynec.*, 52, 598–613, Oct. 1946. 27 refs.

This is a discussion of 2,798 vaginal hysterectomies for benign disease of the uterus. The operation is frequently combined with colpoperineorrhaphy, and the advantages of this are stressed. The author believes that the uterus should be removed by the vaginal route whenever possible. Advantages of the vaginal route are the absence of an abdominal incision and the decreased risk of pulmonary complications of thrombophlebitis, and of bowel complications. Post-operative discomfort

is also less than after abdominal hysterectomy. There is no reason why the vagina should become shorter after vaginal than after abdominal hysterectomy, since the opening into it is made at the same level. Vaginal hysterectomy has been recommended for patients who are poor operative risks, but it seems logical to consider it an even safer procedure than abdominal hysterectomy in patients who are good risks. No definite contra-indications can be laid down, but conditions which obviously make the vaginal route more risky than the abdominal would in general lead to the choice of the latter method. Pre-operative preparation is important and should be directed to clearing up foci of infection, both local and remote, and to correction of anaemia, vitamin deficiency, and poor general nutrition.

The morbidity rate for the whole series, taking as the standard a temperature of over 100.4°F. (38°C.) on any two consecutive days, excluding the first 24 hours, was 36.5 per cent. Causes of morbidity included urinary tract infections, post-operative haematomata, and local infections. The bladder was opened on a number of occasions, and primary suture was performed; vesico-vaginal fistula resulted in 5 cases, and all were eventually cured. Recto-vaginal fistula occurred in 1 case. Prolapse of the Fallopian tube was fairly common; this complication can be dealt with easily by ligating the prolapsed tube and burning it off with the nasal cautery. The average stay in hospital did not exceed 13.5 days. Six patients died (0.214 per cent). This compares very favourably with results as given by other authors. In the summary the need for meticulous haemostasis is again emphasized.

Josephine Barnes

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357. Post-operative Cervical Elongation. (Elongaciones cervicales postoperatorias.) By N. O. DI FONZO. *Rev. méd.-quirúrg. Pat. fem.*, 25, 416–418, Sept. 1946.

358. Accidental Vascular Injection during Hysterosalpingography. (Inyeccion vascular accidental durante la histerosalpingografia.) By A. PIERNES, F. IBARROLA, and E. ROSSELLI. *Rev. med.-quirúrg. Pat. fem.*, 25, 411–415, Sept. 1946. 2 figs.

359. Vaginal Aplasia. Formation of a New Vagina by McIndoe's Technique. (Aplasia vaginal. Formación de una neovagina con la técnica de McIndoe.)

By C. A. Brea and R. C. O'Connor. *Prensa med. argent.*, 33, 2494–2500, Dec. 13, 1946. 7 figs.

360. Modified Sturmdorf Suture. (Modifizierte Sturmdorfnaht.)

By A. H. Palmrich. *Klin. med.*, 1, 601–604, Dec. 1, 1946. 4 figs.

361. The Modern Technic of the Le Fort Operation.
By R. Tauber. *Ann. Surg.*, 125, 334–340, Mar. 1947. 3 figs., 44 refs.

See also Nos. 321, 332, 334, 339

Urology

362. Urology in Women. (Contribución al estudio de la urología en la mujer.)

By J. Falconi Mejia. *Rev. méd. peruana*, 19, 247–304, May 1946.

363. The Problem of Stress Incontinence and its Surgical Relief.
By W. E. Studdiford. *Surg. Gynec. Obstet.*, 83, 742–750, Dec. 1946. 9 figs., 20 refs.

The problems here considered are the surgical relief of patients when a previous operation for stress incontinence has failed and the avoidance of such failures. Forty-four cases have been operated on by the technique here described, of which 13 have already been reported. They include a case of congenital urethrocele and one occurring in a nulliparous patient of 70 years of age, the remainder being the more or less remote effects of childbirth. A review of available labour records revealed that in a surprisingly large number delivery had taken place without obvious injury; it is suggested that efforts to preserve the perineum may result in forward projection of the presenting part and consequent injury to the urethral attachments.

The operation here described and advocated (with admirable illustrations) is a modification of the Aldridge technique, in which a strip of rectus fascia is used to reinforce the pubo-cervical fascia supporting the urethra. In this operation a strip of rectus fascia is used in such a way as to form a sling supporting the urethra; both ends of the strip are fixed just above the symphysis. The operation is done in two stages with one change in position. *Stage I* is performed with the patient in the lithotomy position. Details are given of each step of the operation; as in the operative repair of cystocele,

vaginal flaps are formed extending to the base of the urethra, and the pubo-cervical fascia is divided in the line of the vaginal incision; flaps of this fascia about 2 cm. wide are formed on each side. The plane between the vaginal flap and the fascial flap on each side is dissected up by the finger and extended upward, behind and to each side of the symphysis. The lateral fascial attachment is ruptured by the finger, which then enters the space of Retzius lateral to the bladder neck. There is some venous bleeding during this blunt dissection; it is said to be easily controlled by pressure. At this point the pubo-cervical fascial flaps are approximated by mattress sutures in such a way as to elevate the bladder neck behind the symphysis. When the line of sutures is completed, one end of a rubber tube (Penrose drain), about 30 cm. long, is placed in the space of Retzius on the left side, the other end being pushed by means of forceps into the corresponding space on the right side. The vaginal flaps are now trimmed and closed by a line of sutures, care being taken to avoid the underlying Penrose drain. For *Stage II* the patient is placed in the dorsal position. A midline incision is made from the symphysis to just above the umbilicus and a strip of rectus fascia, with its attached base below and to the left, is formed corresponding in length to the abdominal incision. Care must be taken at the levels of tendinous intersection so that the strip is not weakened during the dissection. The bladder is freed from the upper aspect of the symphysis, and the ends of the Penrose drain are located. The free end of the strip is fixed by suture to the left end of the drain and the strip is drawn through by traction on the other end of the drain. The strip is fixed to the right rectus sheath by a few sutures, care being taken that the sling so formed is not drawn too tight. The abdominal wound is then closed in layers. Generally it is not necessary to open the peritoneum. Post-operatively sulphadizine 0.5 g. is given 4 times a day until the catheter is removed. This is generally done on the ninth day, but normal urination is often delayed and the catheter may have to be re-inserted. In spite of a few failures, the results are regarded as satisfactory, especially in view of the fact that many of the cases had been previously operated upon.　　　　*T. C. Clare*

Sedation with Rectal Tri-brom-ethanol (Avertin, Bromethol) in the Management of Eclampsia

BY

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INTRODUCTION

THE aetiology of eclampsia still evades detection, and the basis of treatment, therefore, remains unsatisfactory. The complete absence of any specific therapy compels the adoption of treatment based either on the relief of the individual clinical manifestations of the disease or upon the various and unproved theories of the cause. Of these procedures the greatest reputation belongs to the sedative management associated with the name of Stroganoff; to the eliminative method at one time so popular in Dublin, and to combinations of these two procedures. It is true that sedation and elimination cannot be regarded as completely compatible one with another, but the attempt to combine them was at one time commonly practised. [The authors of this paper, however, have completely abandoned the so-called eliminative management.] The results of a purely surgical approach to the disease have not been impressive. The condemnation of methods of *accouchement forcé* in the management of eclampsia—as in other spheres—is now universal, and Caesarean section has a somewhat sinister reputation.

The choice of sedative in eclampsia is comparatively restricted. The quick effect of chloroform has led to its occasional use despite its well-known dangers, but for more prolonged sedation the choice has fallen in general upon morphia, certain barbiturates, chloral and paraldehyde. The authors' experience with these drugs has not been wholly satisfactory, since it has not been possible with any certainty to prevent recurrence of seizures, and since dangerous respiratory depression of mother and child has been common when the drugs were pushed. One of us (J. B. D.), impressed by the admirable pre-anaesthetic sedation obtained by the use of tri-brom-ethanol, conceived the idea of using it in eclampsia. Originality cannot be claimed for this use of the drug by either of the authors, but both have been using it si

1943 in two hospitals which together admit virtually all obstetrical emergencies occurring in the counties of Ayr, Dumfries, Kirkcudbright and Wigtown (population approximately 500,000), and they believe that their results have been sufficiently favourable to justify this presentation.

LITERATURE

Tri-brom-ethanol, first introduced as a basal anaesthetic, was later employed as an obstetrical analgesic. Its physical, chemical, and pharmacological properties have been repeatedly described and it is not proposed to recapitulate them.

The use of the drug as an anticonvulsant in tetanus appears to have been suggested early (Läwen, 1927, 1928; Huntingdon, 1931; Sartorius, 1933; Boyce and McFetidge, 1935; Mitchell, 1935; Cole, 1935; Feeman, 1936), and the literature includes statements of its use in eclampsia, of which we have been able to trace those by Conrad (1927), Benhline (1927), Sennewald (1928), Ripley and Cairns (1930), Pierce (1931), Ghlan (1931), Morrison (1931), Whitaker (1933), Carré and Gellé (1938), Gellé (1939), and Miller (1944). There does not appear to have been any publication which included any series of cases sufficiently large to warrant the drawing of statistically significant conclusions, most of the references quoted being descriptions of comparatively few cases with favourable results, without any attempts to produce comprehensive surveys of all cases treated in the clinics concerned.

CASES PRESENTED IN THE PRESENT SURVEY

The patients were drawn from the counties already enumerated. With few exceptions the Ayrshire cases came from an industrial population, the remainder from a mainly agricultural area.

Since January 1st, 1943, all cases under the authors' care were treated by tri-brom-ethanol, except for 4 cases (including 1 fatality) short details of which appear in Table I.

TABLE I

Eclamptic patients since introduction of Bromethol treated otherwise and omitted from series.

CASE A Admitted on second day of puerperium with multiple mid-brain plegias following intrapartum eclampsia treated by family doctor. Did not require sedation Mother and child survived.

CASE B Single and immediately fatal seizure followed 12 hours after mid-forceps delivery of patient, who had been under observation for moderate hypertension for 1 month prior to delivery. Death occurred too quickly for any treatment to be instituted. Child survived.

CASE C After 2 eclamptic seizures at home, developed concealed accidental haemorrhage. Judged too collapsed to justify or to require energetic sedation. Treated by artificial rupture of membranes and transfusion, had 1 eclamptic seizure following recovery from shock, but survived. Baby stillborn.

CASE D Admitted at term in labour, with severe pre-eclampsia, with head on perineum. Developed one eclamptic convulsion. Delivered immediately by low forceps under general anaesthesia. Further seizures judged unlikely, no sedation given. Both survived.

A total of 44 cases is described. Of these 29 cases were treated in Ayrshire, 15 in Dumfries. Although journeys by ambulance were often long and rough, no attempt was made to avoid them, and cases were eventually admitted to hospital.

Full details of individual cases will be found in Table II.

TECHNIQUE OF ADMINISTRATION

*Dosage and Dispensing of Tri-brom-
    ethanol.*

Initial dose. When the weight of the patient has been known, the dosage of fluid "bromethol" has been calculated on the basis of body-weight, using the mean of the recommended basal anaesthetic dosage (i.e. 0.1 ml. of concentrated bromethol solution, as dispensed by manufacturers, per kg. of body-weight) and the recommended "obstretical twilight sleep" dosage (0.75 ml. per kg.).

No attempt has been made to correct the patient's weight by deducting either the estimated weight of foetus and secundines, or the estimated weight fraction due to excessive obesity or to oedema.

Where the patient's weight has been unknown, it has been the practice to make a very rough estimate of her weight (in stones) and to calculate the dosage to the nearest stone.

The measured quantity of fluid bromethol is added to the necessary quantity of water at 40°C. to make up a final 3 per cent solution, which is then administered by slow rectal injection, after a preliminary Congo Red test to prove the absence of the acid product resulting from overheating.

When the eclampsia has developed outside hospital, it has been our practice to make up bromethol in dosage suitable for a person weighing 12 stones. A house surgeon is sent out to the patient's home with the dispensed solution in a thermos flask, having been instructed to adjust the dosage on arrival in accordance with his estimate of the patient's weight (when this obviously less than 12 stones) by discarding either 10 ml. or 20 ml. of the solution. After such necessary adjustment, the dose administered and 20 minutes later the patient is carried to the ambulance.

Subsequent doses. We were at first timid to repeat the dosage of bromethol, but with increasing experience we have become convinced that there is a wide margin of safety, and now do not hesitate to give repeated doses to any patient showing signs of restlessness. In general, we are quite prepared to give a second dose some 3 hours after the first. Later repeated doses are not infrequently called for, and we do not withhold them, subject to the proviso that we will not give a third or later dose within a period of less than 3 hours of the immediately preceding one; and we prefer if possible to wait even longer. Quite often patients sleep quietly for 6 to 12 hours following the second dose, and the third dose, if then given, will often enable a peaceful 24 hours to be completed. We believe that it is rarely necessary to maintain sedation for longer than this period.

Difficulties in administration. It is remarkable how seldom there is serious difficulty in administering the rectal injection, despite the fact that eclamptic patients are notoriously restless. The injection is fortunately of small bulk, and a skilful nurse can often insert the rectal catheter without much discomfort to the patient who, if her head be kept low, will then usually retain a slowly given injection.

After the withdrawal of the rectal catheter a patient will sometimes expel a small quantity of the fluid, recognised by its characteristic aromatic odour. This can generally be neglected, for the drug takes effect in some 20 minutes and, if it be retained for more than half an hour, the loss of quite large quantities has comparatively little effect in shortening the duration of action. In some cases we have given an extra half dose of the drug at once on the escape of any large quantity of fluid quickly following the initial injection.

Patients in the late second stage of labour

give difficulty owing to the pressure of the presenting part. When further sedation is indicated at this time, and natural delivery does not appear imminent, it is quite justifiable to terminate labour under general anaesthesia by operative means, after which the patient can be given the desired dose of bromethol during recovery from the anaesthetic. In passing, it may be noted that persistent relaxation of the anal sphincter following delivery under spinal anaesthesia may make it impossible for the injection to be retained.

On one occasion a patient developing eclampsia at home expelled the greater quantity of her initial dose in the ambulance on the way to hospital. On admission she was extremely restless and disorientated, and required very firm restraint. It was quite impossible to attempt a further rectal injection, but the patient was completely subdued by 0.25 g. of intravenous sodium pentothal, following which the original dose in full was administered with good effect. This woman did well.

DANGERS OF BROMETHOL

In the dosage that we have employed we have not seen any clinical evidence of liver damage, nor of any undesirable side effects other than bronchitis. None of the cases of bronchitis has been in any way alarming and the incidence does not appear to have been any higher than after other methods of management of eclampsia.

We have been fortunate in the rather short series we describe not to have encountered a case with anuria, although in several cases a more or less pronounced oliguria occurred. We do not consider that the bromethol was in any way responsible for the oliguria. We do not have information as to the possible results of giving bromethol to a patient in established anuria, although, since the drug is excreted by the kidneys,

prolonged effect from a single dose might well be anticipated.

CONTRA-INDICATIONS TO BROMETHOL

The only contra-indication we have accepted in the present series is in respect of a single patient whose eclampsia was complicated by concealed accidental haemorrhage with marked shock (Case C in Table I).

So far as the second and subsequent doses of bromethol are concerned, we recognise the detection, by extra auscultation, of moist sounds in the respiratory passages as an indication to delay repeating the dose until the cough reflex is active. We have overridden this consideration, however, in a few cases where the clinical appearance of the patient suggested that a seizure might be imminent.

CONCURRENT OBSTETRIC MANAGEMENT.

Antepartum eclampsia. Following the first dose of bromothol, a vaginal examination is made and, where the finger can be passed through the cervical canal, it is our practice at once to rupture the membranes artificially. Where the cervical canal cannot be penetrated by the finger, or when the cervix is unduly long or firm, we generally avoid rupturing the membranes. In such cases an endeavour is made to assess the severity of the case from the clinical findings. If the case seems to be mild we adopt a purely conservative *régime*, performing induction of labour 24 to 48 hours after the eclamptic crisis appears to have passed. When the case is judged to be a severe one we give full consideration to the desirability of Caesarean section, which can usually be carried out successfully with local anaesthesia to supplement the bromethol. We interpolate the observation that in our very small series of cases we have treated ...

bromethol we have not been in any way alarmed by the subsequent progress of the few patients delivered by Caesarean section.

Intrapartum eclampsia. Prior to the natural completion of cervical dilatation we have confined ourselves to artificial rupture of the membranes designed to accelerate labour.

In the second stage of labour we have not made any definite rule requiring operative delivery as a routine, but when eclampsia has developed for the first time towards the end of the second stage, we have usually completed vaginal delivery by operative means under general anaesthesia before commencing bromethol sedation. Apart from this we have not felt obliged to shorten the second stage except in women who were becoming restless despite sedation, or for definite mechanical indications.

The details of obstetrical management in individual cases are recorded in Table II.

RESULTS.

(a) *Mortality.* The results are tabulated in Table III.

It is unfortunate that contemporaneous controls are not available from this district, but the figures for the years 1939 to 1943 are quoted for comparison.

(b) *Incidence of fits.* Apart from our earlier cases, when we were somewhat timid in repeating the dosage of bromethol, we have found it rare for fits to recur once treatment has been started. Of the total number of 44 cases, fits occurred following commencement of bromethol in 3 only. In only 1 of these was there more than a single recurrent seizure. The detail of individual cases is shown chronologically in the accompanying diagram (Fig. 1)

Again, no contemporaneous controls are available, but the incidence of fits in the 88 cases treated by sedatives other than bromethol is plotted in Fig 2, while a comparative diagram showing the percentage of patients having recurrent seizures is demonstrated in Fig. 3.

(c) *General effect upon patient.* Within 20 minutes of the first injection the patients became quite quiet, with tranquil breathing. The colour remained good in all cases Respiratory embarrassment was restricte to palatal stridor. No patient was observe to vomit. Where the blood-pressure hav been seriously elevated a sharp fall w invariably noted.

(d) *Effect upon labour.* Most cases d not show any interference with the norm course of labour, apart from a poor use the abdominal muscles.

(e) *Effects upon child.* Serious apno was rarely observed in babies whose hea were still beating on delivery. No case neonatal death could be attributed to th method of sedation. We have made attempt to provide a "corrected" figu for foetal mortality but, from the sh details provided in Table II, it will apparent that prematurity played a while there was one case of hydrocep

	Bromethol cases	Cases otherwise managed
	1943–46	1939–43
Number of patients treated	44	88
Number of babies delivered	49	82
Number of abortions	2	1
Maternal deaths	2 (4.5 per cent)	*18 (20.5 per cent)
foetal deaths:		
Stillbirths	7	23
Neonatal deaths	8	11
Total	15 (30.6 per cent)	34 (41.5 per cent)

TABLE III.

* Includes 8 undelivered
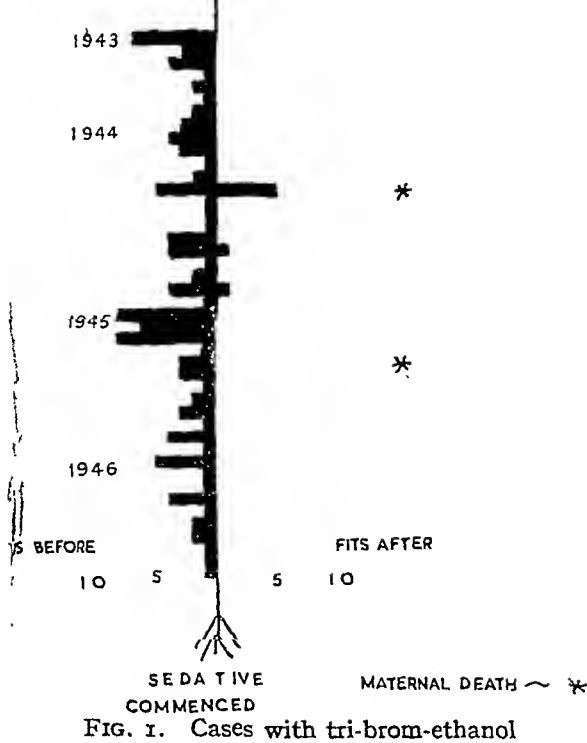
FIG. 1.   Cases with tri-brom-ethanol

SEDATIVE COMMENCED

MATERNAL DEATH ~ *

1943

1944

1945

1946

FITS BEFORE

FITS AFTER

10   5   5   10

40.7%

NO FITS

93.2%

NO FITS
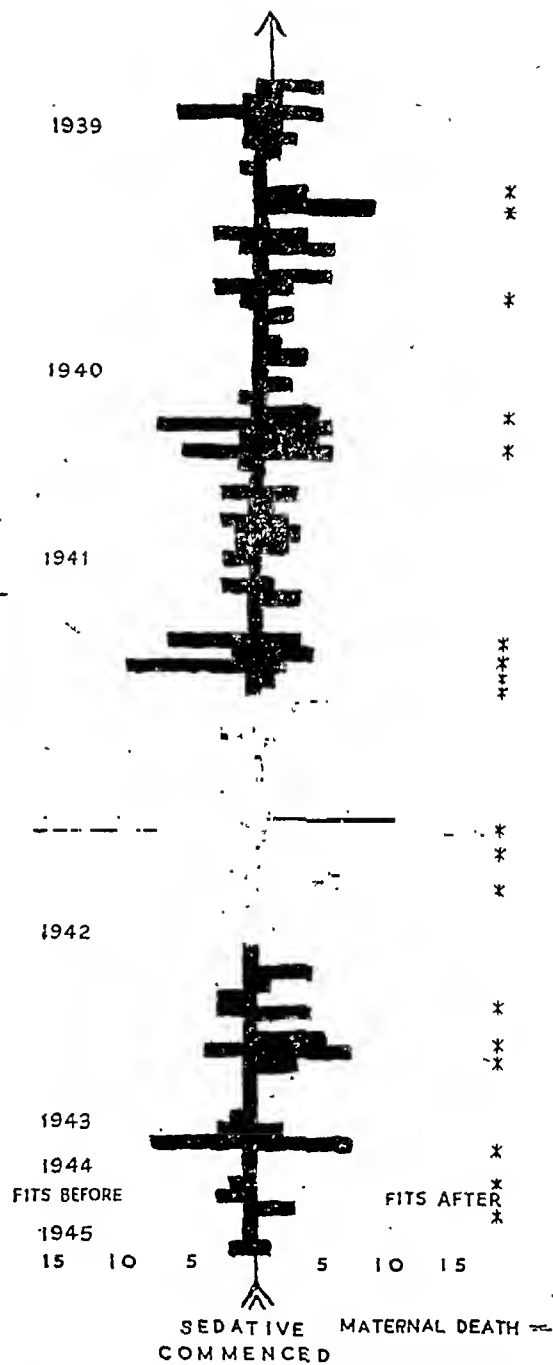
Tri-brom-ethanol

FIG. 2.   Cases without tri-brom-ethanol

SEDATIVE COMMENCED

MATERNAL DEATH ~

1939

1940

1941

1942

1943

1944

FITS BEFORE

1945

FITS AFTER

15   10   5   5   10   15
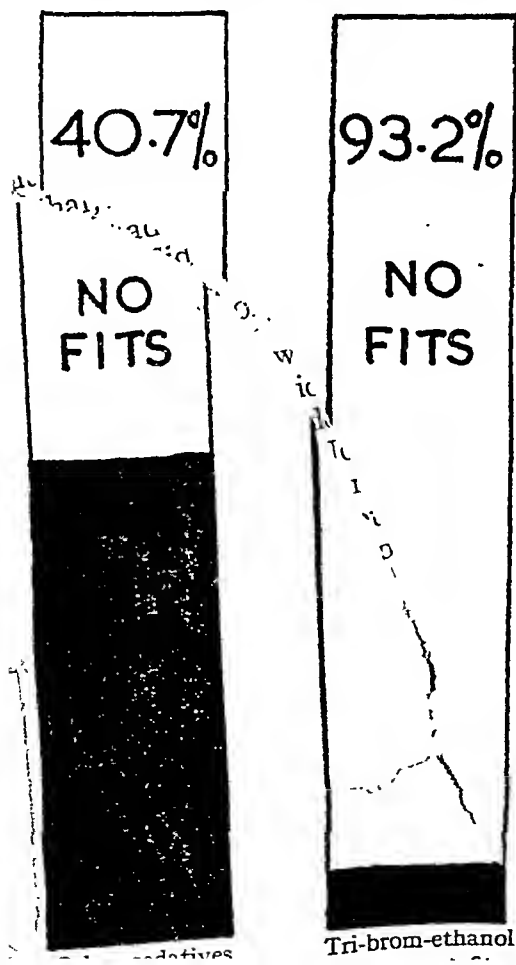
(f) Short notes of maternal fatalities.

CASE 13, Table II. Age 23; 2-para; unbooked; no antenatal care.

Postpartum eclampsia.

Admitted in deep coma with restlessness 7½ hours after spontaneous delivery of a living 7 pounds 4 ounces child at term. The first fit had occurred 4 hours after delivery, with a total of 6 seizures prior to admission, all described as " very severe "; temperature 98°F.; pulse-rate 136; respirations 22, with extreme stertor; blood-pressure 170/100; moderate oedema; albuminuria of 800 mg./100 ml.; urinary output uncertain owing to incontinence. Bromethol, 5.3 ml. in appropriate dilution, failed to subdue restlessness completely, and repeated doses (of 3.0 ml. only) were administered 2, 4, and 12 hours after the first, these later doses being reduced because of continuing coma with absent reflexes. There was no further restlessness after the fourth dose, but the pulse-rate became progressively more rapid, the temperature rose to 103°F. and unconsciousness persisted. Further bromethol was considered inadvisable. Twenty-four hours after admission, that is, 12 hours after the final dose of bromethol, one short fit developed. Twenty hours later 3 fits in rapid succession occurred. Lumbar puncture at this time yielded clear cerebro-spinal fluid under normal pressure. The patient died 72 hours after delivery without regaining consciousness. Venous blood taken 24 hours prior to death showed urea, 199 mg. per 100 ml. Permission for autopsy was refused. The child survived.

Obviously this was a very severe case and the fact that no fits occurred for 24 hours after commencing bromethol sedation may possibly be taken to indicate the effectiveness of the method. Whether the outcome could have been influenced favourably by continuing the treatment seems doubtful, but it may be claimed with some reason that the fatal result was not attributable to the action of the drug.

CASE 27, Table II. Age 33; 2-para; unbooked; antenatal care perfunctory.

Antepartum eclampsia.

This woman was admitted to hospital after 3 seizures. Blood-pressure 190/120; moderate oedema; heavy albuminuria. There were no fits after commencement of sedation by bromethol. Labour was induced by puncture of the membranes. Twelve hours after admission the patient was delivered spontaneously of binovular twins (1) boy, 6 pounds 13 ounces; (2) girl, 6 pounds 5 ounces. The woman recovered consciousness and the puerperium was entirely satisfactory until the fifth day, when she died very suddenly, apparently from acute heart failure (? pulmonary embolus). Permission for autopsy was refused. Both children survived.

The control of the eclampsia in this case was complete, and it seems improbable that the fatal outcome can be in any way connected with the sedative employed.

DISCUSSION.

The figures in this series in respect of maternal and foetal mortality are a distinct improvement upon those of the preceding years in the same area. They are also rather better than the average figures quoted for mortality in eclampsia in the annual reports of Scottish hospitals. However, the series is small, and there have not been synchronized control cases in the authors' hands. It would therefore be impertinent to claim that the improved figures are statistically significant.

Whilst there is no convincing evidence of diminution in the numbers or the severity of cases of eclampsia, there is an increasing tendency to transfer to hospital immediately all patients developing seizures at home or in nursing homes. The effect is undoubtedly to bring the eclamptic patient much more speedily under hospital control and, accordingly, better results are to be anticipated independently of the method of sedation adopted.

At the same time it would probably be unfair to describe the cases in the bromethol series as exclusively of a mild type. It is true that, judged by the number of fits

they do not appear very severe; but we believe that the excellence of the sedation has been a misleading factor in this respect. As judged by the criteria of blood-pressure, albuminuria and oliguria the cases have not been mild, and our impression is that in a number of them fits would have been frequent and severe had we employed a less effective agent.

However, although we do not feel justified in claiming that management of eclampsia with bromethol will yield mortality-figures greatly differing from those obtained with other sedatives, we do strongly put forward our belief that bromethol is a very powerful anticonvulsant and is of particular value in eclampsia. The very low incidence of seizures following the institution of treatment is highly suggestive of this. The ease of handling patients under the influence of bromethol is also striking. It is quite unnecessary to resort to anaesthesia for control during catheterization or any other nursing attention, and the patients are not resentful of the changes of posture so desirable in the nursing of eclampsia. They are also tolerant of bright light, and noise does not disturb them except when the effect of the dose is beginning to wear off. They can be transported very easily under the influence of bromethol. No case has developed fits in the ambulance despite some long, rough journeys.

In our joint experience of close contact with eclamptics over the whole course of their illness we have recollection of no series of cases in which we were less anxious about the patients, and in which the patients were easier to handle.

We have come to have such great confidence in the effects of bromethol that we are now disposed to take a much more conservative view of the management of pre-eclampsia. We believe that in bro-methol we have a sedative agent which enables us to persevere with conservative treatment, even in the presence of urgent prodromal symptoms of eclampsia, since we can confidently expect to control any seizures which do actually develop. We realise that the severity of eclampsia is controlled by factors additional to the number of fits and that it is unlikely that these factors will be influenced at all favourably by bromethol, possibly the reverse. Nevertheless, this trust in our sedative agent has given us added confidence in the handling of these difficult cases.

In parenthesis, we think it permissible to refer to the fact that in many cases of severe pre-eclampsia we have used bromethol in the initial treatment and during labour, and that no case has developed fits when under its influence. We have also used bromethol from time to time as an analgesic in normal labour, but are not so favourably impressed with it in this field. Sedation has seemed to us more difficult to achieve than in the eclamptic. We do not wish to decry bromethol in this respect, but in our hands it has proved erratic.

SUMMARY

1. Details of a series of 44 eclamptics from South-West Scotland are given.

2. All cases recorded were managed by sedative treatment using rectal tri-brom-ethanol (Avertin, Bromethol).

3. Attention is drawn to the favourable course of these cases with regard to the control of fits.

4. Maternal mortality in cases so treated was 4.5 per cent.

5. Foetal mortality was 30.6 per cent.

those obtained.   We are much indebted to Messrs. Bayer and Co., Messrs. British Drug Houses Ltd., and Messrs. Burroughs Wellcome and Co., for help with references to the literature.

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The Excretion of Drugs in Human Milk—A Review

BY

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FROM time to time information is sought with regard to the excretion of drugs in human milk. No comprehensive account appears in the literature. There are in the main but scanty isolated reports. Many of the older statements are not based on accurate scientific or chemical investigation and are valueless. Only occasional investigations have been made owing to the difficulties involved. In recent years more thorough studies have been made with regard to a few drugs, especially the sulphonamides. Here chemical analyses have been made on a fair number of lactating women, and often correlated with other findings such as the corresponding levels in the blood.

In the following review the medical literature in the English language has mainly been consulted. It will be noted that there is no information at all on the excretion of many substances used in therapeutics, and details about others on which reports have been made are very inadequate. There is still scope for research on this subject, which will increase with the rapid introduction of new therapeutic agents.

One of the earliest reviews of this subject was made by Reed (1908) many of whose observations still hold good to-day. The fact that it is practically never necessary to remove the child from the breast when the mother is receiving drug therapy is borne out by the rarity of cases of untoward reactions reported in the literature. Another important point that still holds is that it is rarely if ever desirable to treat a child with drugs given to the mother. From the clinical and qualitative chemical evidence at that time Reed concluded that alcohol, opium, chloroform, ether, thyroid, and lead are to be used with care, and that atropine, antipyrine (phenazone), phenacetin, chloral, arsenic, bismuth, mercury, copper, castor oil, senna, quinine, bromides, iodides, salicylic acid, and copaiba, pass into the milk in small quantities. An almost identical list is given by Stander (1941).

In the account presented here the reports since 1908 have been studied. The vitamin content of human milk has not been considered.

CENTRAL NERVOUS DEPRESSANTS.

Alcohol. The milk may contain a small amount of alcohol if large quantities are ingested, but not with ordinary doses (Sollmann, 1942). While the maximum amount excreted has been regarded as too small to affect sucklings, a case of poisoning in a breast fed infant 8 days old has been reported (Bisdom, 1937). The mother consumed 750 g. of port. The child was in deep sleep from which it could not be wakened. Alcohol was found in the blood of the mother and child.

Chloroform. According to Scanzo quoted by Reed (1908), a newborn child whose mother had been given chloroform

for after-pains, stopped suckling after a short while on the breast and remained in a deep sleep for 8 hours.

Barbiturates. Excretion of barbiturate into breast milk has been demonstrated, but the amount is generally too small to affect the infant. Kwit and Hatcher (1935) could find no evidence of barbitone 6 hours after the administration of doses of 650 mg. (10 gr.). These authors doubted whether in a report made by Frensdorf (1926) phenobarbitone was the cause of depression in an infant whose mother had taken 0.8 g. of the drug in 3 days.

Tyson *et al.* (1938) found the amount excreted is somewhat greater when the barbiturate is given in a single dose than when it is distributed.

A small amount of barbiturate was found in the milk by Mayo and Schlicke (1942) after an injection of 1125 mg. pentothal sodium; the concentration was higher than in the blood.

Chloretone. Blanner (1919) stated that this drug is found in the milk only with continuous administrations of very large doses. With doses of 5 to 20 gr. he found no trace even with doses repeated several times. No antigalactogogic effect was observed such as can be produced with relatively larger doses in lactating dogs.

Bromides. This is well known as a possible cause of a skin eruption in infants; example, Van der Bogert (1921) found more than traces " in the milk which ed a papulopustular eruption.

wit and Hatcher (1935) found sodium mide in the milk of mothers given 1 g. mes daily for 3 days; in one specimen 120 ml. there were 8 mg. of the drug.

Tyson *et al.* (1938) found that the amount excreted may have a sedative effect on the infant.

Morphine. Talbot (1914) stated that orphine had not yet been found in human milk. Terwilliger and Hatcher (1934) found no alkaloid in the milk of an addict taking 20 gr. of morphine sulphate daily, while in a normal woman given 16 mg. of this drug a trace may have been present in the milk 7½ hours later. In another investigation no alkaloid could be detected with certainty by Kwit and Hatcher (1935) 4 hours after subcutaneous injection of 16 mg. of morphine sulphate.

Codeine. None of the alkaloid was recovered 4 hours after single doses of 65 mg. nor after 6 doses of 32 mg. given every 4 hours (Kwit and Hatcher, 1935).

AUTONOMIC DRUGS.

Atropine. Paterson and Smith (1938) state that atropine is not excreted in the milk. It is well known that belladonna or its alkaloid atropine markedly diminish the milk flow (Stander, 1941), and the drug transmitted through the milk may affect the child.

Hyoscine. This alkaloid is rapidly destroyed in the tissues and only minute traces appear in the milk; thus there should be no danger in prescribing it for a nursing mother, for example when used to prevent seasickness (*Brit. Med. J.,* 1946).

Nicotine. Tobacco is being smoked by women on an increasingly large scale. The problems in connexion with this habit that have been investigated are (*a*) whether the important constituent, nicotine, is excreted in the breast milk, (*b*) whether the infant can be affected by nicotine in the milk, and (*c*) whether lactation itself is affected.

Hatcher and Crosby (1928) found that large doses suppress the secretion of milk in the cat and the cow. In one woman who smoked 20 to 25 cigarettes daily for 6 days the milk secretion became reduced; using the frog method they found less than 0.015 mg. of the alkaloid in some milk (about 26 ml.) collected after 7 cigarettes

had been smoked in 2 hours. Chiasson (1929) found good lactation in French families where the women were regular pipe smokers.

Emanuel (1931) in a study on 10 patients found nicotine in the milk, sometimes 1 or 2 hours after smoking, but the main excretion was after 4 or 5 hours, and in some cases was still demonstrable 7 to 8 hours after smoking. Leech segments were used for estimating the nicotine and by this method a maximum of 0.03 mg. per litre of milk was found after the smoking of 7 to 15 cigarettes, an amount below the toxic threshold.

Thompson (1933) also found nicotine in breast milk. He stated that he had not observed a patient smoking 8 or more cigarettes daily whose lactation was adequate at 3 months after delivery.

Nicotine intoxication in factories or from excessive smoking may affect the mother and also the child.

Poisoning has occurred in a breast fed infant 6 weeks old. The mother smoked 20 cigarettes a day and her milk contained nicotine. The symptoms were restlessness, insomnia, "spastic" vomiting, diarrhoea, rapid pulse, and circulatory disturbances; recovery occurred with symptomatic treatment (Bisdom, 1937).

In a recent study Perlman, Dannenberg and Sokoloff (1942) using *Daphnia magna*, a fresh water crustacean, as test organism, found nicotine in every specimen of milk obtained from 55 mothers who smoked varying numbers of cigarettes, from 1 up to 20 or more over a 12-hour period. By this method higher values, average 0.116 to 0.5 mg. per litre of milk, were obtained than in the case of Hatcher and Crosby (1928) and Emanuel (1931) mentioned above. They concluded that lactation and the nursling were little if at all affected by the nicotine, due to the development of tolerance for the drugs, especially as all the mothers had smoked before.

PURGATIVES.

Phenolphthalein. None of the drug was detected after administration of a dose of 90 mg. (1½ gr.) (Kwit and Hatcher, 1935).

According to Fantus and Dyniewicz (1936) no free phenolphthalein is excreted in the milk within 24 hours or more of taking large doses (0.2 to 0.8 g.) of phenolphthalein. Minute quantities of conjugated phenolphthalein may be found. No obvious effect on the bowel movements occurred in the infants of mothers taking phenolphthalein.

Emodin. This is the active constituent of senna, cascara, rhubarb, aloes. A certain amount is absorbed and may produce purgation in the suckling (Sollmann, 1942). Tyson *et al.* (1937) found no evidence of phenolphthalein, calomel, senna, or rhubarb on chemical analysis. Aloin was transmitted in too small amount for laxative action in the child. Cascara gave both chemical and clinical evidence of transmission.

ANTIMICROBIAL AGENTS.

Sulphonamides. Sulphanilamide may be found in the milk in both the free and the conjugated form and is present for days after administration has ceased. In an investigation on 20 subjects Adair, Hesseltine, and Hac (1938) found 3.76 to 13.67 mg. sulphanilamide in the milk after doses of 2 g. and 11.77 to 54 mg. after doses of 4 g., a variation of 0.006 to 0.016 and from 0.019 to 0.04 mg. per ml. The drug was present in both free and acetylated forms, and the level was much higher in the milk than in the blood.

In a later study Hac, Adair, and Hesseltine (1939) gave 25 normal lactating women

2 to 5 g. of the drug in 6 doses daily for 3 days. The drug was still found in small amount 48 hours after administration was stopped. The percentage of drug excreted as the conjugated acetyl form varied from 35.1 to 83.9. The total amount excreted during 5 days was never greater than 0.23 g. or 1.6 per cent of the amount ingested, too small to be dangerous to the infant.

Stewart and Pratt (1938) found that after 2 g. of sulphanilamide the concentration of free drug in the milk corresponded to levels in the blood (2 to 4 mg. per 100 ml.), and after 4 g. doses the concentration was equal to or slightly higher than the blood level of 4 to 7 mg. per 100 ml. No toxic effects occurred in babies drinking the milk; traces of the drug were present in the blood and urine of the baby.

Pinto (1938) found the concentration of sulphanilamide after a single large dose of 4 g. followed the concentration in the blood, but lagged behind by a few hours. Hepburn, Paxson, and Rogers (1938) gave a daily dose of sulphanilamide of 1.6 g. (0.3 g. every 4 hours) and found the free drug in the milk 24 hours later in a concentration between 0.55 and 2.17 mg. per 100 ml. Where the mothers received sulphanilamide for several additional days, the drug was found in the urine of the infants in concentration varying from 0.19 to 1.4 mg. per 100 ml. In a later investigation these workers (Hepburn, Paxson and Rogers, 1942) found 0.5 to 2.7 mg. per 100 ml. milk of the free form and 0 to 7.2 of the conjugated form, total 1.9 to 9.4; in the urine of infants obtained at the same time there was 0.5 to 2.7 of free sulphanilamide, 0.9 to 21.7 of conjugated form, with a total of 1.3 to 25 mg. per 100 ml.

Foster (1939) reported the excretion of sulphanilamide in the milk.

Aguirre and collaborators (1942) have determined the excretion of various sulphonamide compounds in milk.

When sulphathiazole was given in daily doses of 3 g. Rieben and Druey (1942) found 0.5 to 1.5 mg. of the free form per 100 ml. milk, and after doses of 6 g. daily 1 to 2 mg., the corresponding blood levels being 2 to 3 times this amount. The infant received not more than a total daily amount of 4 mg.

Penicillin. Greene, Burkhart, and Hobby (1946) found penicillin in the breast milk in small amounts (0.015 to 0.06 unit per ml.) the blood levels ranging from 0.112 to 1.92 units per ml. following intramuscular injection of doses of 100,000 units.

Mandelic acid. In a study on 6 mothers (and their infants) Berger (1941) found that when 12 g. mandelic acid are given daily from the first day of delivery and with the daily fluid intake restricted to 1,200 ml. the amount in samples of the breast milk varied considerably. The estimated average amount of the drug excreted in 24 hours was 0.2726 g. Thus the infants never get a dangerous amount of the drug.

Hexamine. According to Sollmann (1942) this substance has been found in the milk; the highest concentration was reached after an hour .

Arsphenamine (Salvarsan). According to Paterson and Smith (1938) salvarsan is not excreted in the milk.

OTHER SUBSTANCES.

Iodide. This was found only in very small amount by Kwit and Hatcher (1935) after total doses of 3.6 (325 mg. were given 3 times daily) and 4.6 (650 mg. 3 times daily) grammes of the potassium salt.

After a dose of 0.6 g. (10 gr.) of potassium iodide, Maurer and Ducrue (1928) found about 68 mg. or 15 per cent of the dose in the milk in 3 days. According to

Sollmann (1942) milk normally contains some iodide, 0.02 to 0.03 mg. per litre.

Fluoride. Small quantities have been found in milk (Sollmann, 1942). This is of interest in view of the effects of fluorine on bone and tooth enamel.

Quinine. Only traces were found in milk by Terwilliger and Hatcher (1934) even after doses of 640 mg. (10 gr.).

Salicylic acid. This could be detected even after giving 10 gr. of sodium salicylate (Kwit and Hatcher, 1935).

Ergot alkaloids. These were found in the milk by Fomina (1934); some infants showed clinical signs of intoxication.

Caffeine. Traces of this substance or a derivative were found in the milk of coffee or tea drinkers (Irvin, 1926).

Schilf and Wohinz (1928) recovered about 1 per cent of the caffeine in milk drawn 6 hours after coffee had been taken.

Radio-active sodium. This substance has been recovered in the milk within 20 minutes of administration, with a maximum concentration in about 2 hours, the subsequent secretion falling slowly with sodium still recoverable after 96 hours (Pommerenke and Hahn, 1943).

Colchicum. According to Garrod *et al.* (1929) this substance may pass into the milk.

Carotene: Consumption of several carrots daily caused carotenoderma (carotenaemia) in a mother and her suckling of 6 months. The yellowness of the infant's skin disappeared when the breast feeding was stopped (Thomson, 1943).

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Calcium and Phosphorus Metabolism in Pregnancy
(A Survey under War and Post-war Conditions)

First Communication on the Temperamental and Emotional Factor

BY

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The present communication deals with a further 17 women, cases 37 to 53, whose calcium intake and output figures are shown in Table I.

The reader is referred to the two previous papers (Obermer, 1946a; 1946b) on this subject for (a) an outline of the investigation as a whole, its scope and objectives; (b) references which cover most of the published work on calcium and phosphorus metabolism during pregnancy, as well as most of the Calciferol literature; (c) calcium intake and output figures of a group of control women (Group I), a group of women given a supplement of calcium phosphate (Group II) and a further group given the same doses of calcium phosphate together with large amounts of Calciferol (Group III).

The figures given in Table I are the calcium intake and output figures of cases 37 to 53, who were on a self-chosen diet, had no calcium phosphate supplement, but were given Calciferol in the following dosage:

Cases 36 and 37.
800 units of D_2 per day throughout pregnancy. (In the form of " Government Capsules ", as distributed at health centres and antenatal departments. Each capsule also contained 97 mg. of calcium and 50 mg. of phosphorus—quantities so small that they can be disregarded as supplements.)

Cases 39 to 41.
1,000 units first 6 months; 2,000 units last 3 months (in the form of Radiostol liquid).

Cases 42 and 43.
3,000 units for first 6 months; 6,000 units for last 3 months.

Cases 44 to 46.
3,000 units up to end of 5th month; 6,000 units 6th and 7th months; 9,000 units 8th month onwards.

Cases 47 and 48.
9,000 units first 6 months; 18,000 units last 3 months.

Cases 49 and 50.
9,000 units up to end of 5th month; 18,000 units 6th and 7th months; 27,000 units 8th month onwards.

Cases 51 to 53.
18,000 units up to end of 5th month; 27,000 units 6th and 7th months; 36,000 units 8th month onwards.

(Cases 43 to 53 had their supplement in the form of Radiostol pellets—3,000 units each.)

Comparison of Calcium and Phosphorus Balances.

The figures for all 4 groups are given in Tables II and III.

If these tables are compared with the similar tables in a previous paper (Obermer, 1946b) it will be seen that a further 16 control or Group I balances have been added. These have been taken from Section 1 of Table I in the present paper and represent the preliminary investigations (before Calciferol supplements were given) together with 3 balances during later stages of pregnancy, when no Calciferol supplements had been taken for

TABLE I.
Tabulation of Calcium Intake and Output Figures.
(The figures on each line represent the findings of a 48-hour period in terms of grammes of calcium element).

Section 1

| Date | Week of pregnancy | Case No. | Calcium intake | | | | | Calcium in blood | Calcium in urine | Calcium in faeces | Total calcium output | Calcium balance |
			Milk	Cheese	Other foods	Sup.	Total					
1. 2.1945	18	37	1.93	Nil	0.37	Nil	2.30	10.7	0.77	0.62	1.39	+0.91
7. 5.1945	30		1.94	Nil	0.34	Nil	2.28	9.7	0.48	0.56	1.04	+1.24
8. 7.1945	24	39	1.51	Nil	0.37	Nil	1.88	10.0	0.36	2.80	3.16	-1.28
10.10.1945	38		1.75	0.24	0.30	Nil	2.29	—	1.05	1.82	2.87	-0.58
21. 7.1945	14	40	2.12	Nil	0.73	Nil	2.83	12.1	1.37	1.12	2.49	+0.36
23.10.1945	9	41	1.28	Nil	0.59	Nil	1.87	10.2	0.87	4.60	5.47	-3.60
6. 9.1945	12	42	0.92	Nil	0.21	Nil	1.13	11.4	0.73	1.72	2.45	-1.32
14. 9.1945	9	43	0.61	0.36	0.35	Nil	1.32	10.0	0.34	1.30	1.64	-0.32
4.10.1945	14	44	1.10	0.12	0.79	Nil	2.01	9.8	1.10	3.50	4.60	-2.59
13.10.1945	9	45	1.34	Nil	0.49	Nil	1.83	11.0	0.78	2.85	3.63	-1.80
19.12.1944	15	47	2.00	Nil	0.64	Nil	2.64	10.9	0.89	2.06	2.95	-0.31
14. 5.1945	10	49	1.16	Nil	0.59	Nil	1.75	10.0	0.72	2.25	2.97	-1.22
9. 6.1945	21	50	1.22	0.12	0.58	Nil	1.92	10.4	0.65	1.64	2.29	-0.37
8.11.1945	9	51	1.15	0.12	0.45	Nil	1.72	9.8	0.79	1.62	2.41	-0.69
22. 1.1946	8		1.09	0.61	0.42	Nil	2.12	9.7	0.53	0.72	1.25	+0.87
16. 8.1946	39	53	2.22	0.32	0.33	Nil	2.87	—	0.74	3.20	3.94	-1.07

Section 2

| Date | Week of pregnancy | Case No. | Calcium intake | | | | | Calcium in blood | Calcium in urine | Calcium in faeces | Total calcium output | Calcium balance |
			Milk	Cheese	Other foods	Sup.	Total					
22. 3.1945	24	37	1.76	Nil	0.45	0.19	2.41	11.0	0.45	1.30	1.75	+0.66
16. 6.1945	36		0.85	0.12	0.64	0.19	1.80	9.9	0.44	2.16	2.60	-0.80
13. 6.1945	17	38	1.76	Nil	0.49	0.19	2.44	9.7	0.40	0.93	1.33	+1.11
26. 7.1945	23		1.28	0.48	0.40	0.19	2.35	9.4	0.64	1.53	2.17	+0.18
12. 9.1945	30		1.57	0.48	0.54	0.19	2.78	10.5	0.83	2.07	2.90	-0.12
25. 8.1945	31	39	1.44	0.12	0.31	Nil	1.87	10.2	0.97	1.68	2.65	-0.78
24.10.1945	40		1.77	Nil	0.36	Nil	2.13	—	0.76	1.00	1.76	+0.37
5. 9.1945	20	40	1.34	Nil	0.47	Nil	1.81	11.4	0.63	2.20	2.83	-1.02
12.10.1945	26		1.15	Nil	0.66	Nil	1.81	11.9	0.49	2.09	2.58	-0.77
29.11.1945	31		0.58	0.27	0.72	Nil	1.57	10.1	0.63	1.25	1.88	-0.31
6.12.1945	15	41	1.24	0.69	0.71	Nil	2.64	9.8	0.78	2.23	3.01	-0.37
24. 1.1946	21		1.60	0.69	0.60	Nil	2.89	9.6	0.92	2.05	2.97	-0.08
8. 3.1946	27		2.36	0.97	0.45	Nil	3.78	10.6	1.03	3.94	4.97	-1.18
16.10.1945	18	42	1.62	0.20	0.23	Nil	2.05	11.0	0.45	0.97	1.42	+0.63
29.11.1945	24		0.90	Nil	0.34	Nil	1.24	9.7	0.42	0.80	1.22	+0.02
15. 1.1946	31		1.22	Nil	0.21	Nil	1.43	10.0	0.56	0.80	1.36	+0.07
19.10.1945	15	43	0.58	Nil	0.63	Nil	1.21	9.6	0.39	1.70	2.09	-0.78
29.11.1945	21		0.53	0.36	0.59	Nil	1.48	10.4	0.37	2.40	2.77	-1.29
15. 1.1946	28		1.48	Nil	0.76	Nil	2.24	10.7	0.25	1.96	2.21	+0.03
26. 2.1946	34		0.68	Nil	0.87	Nil	1.55	10.6	0.32	2.00	2.32	-0.77

B

Date	Week of pregnancy	Case No.	Calcium intake					Calcium in blood	Calcium in urine	Calcium in faeces	Total calcium output	Calcium balance
			Milk	Cheese	Other foods	Sup.	Total					
27.11.1945	21	44	1.68	Nil	0.95	Nil	2.63	10.2	0.78	4.30	5.08	−2.45
17.1.1946	28		1.52	0.27	0.67	Nil	2.46	10.4	0.72	1.15	1.87	+0.59
28.11.1945	15	45	1.52	0.27	0.53	Nil	2.32	9.7	0.79	2.60	3.39	−1.07
18.1.1946	22		1.64	0.40	0.42	Nil	2.46	10.6	0.89	2.50	3.39	−0.93
28.2.1946	28		1.81	Nil	0.41	Nil	2.22	9.8	1.36	5.39	6.75	−4.53
12.4.1946	34		2.36	0.56	0.51	Nil	3.43	10.4	0.57	5.15	5.72	−2.29
24.10.1945	11	46	1.70	0.20	0.27	0.19	2.35	10.8	0.82	1.31	2.13	+0.23
7.12.1945	17		1.29	0.12	0.37	0.19	1.97	10.4	0.69	2.50	3.19	−1.22
29.1.1946	23		1.34	0.44	0.51	0.19	2.48	—	0.47	2.26	2.73	−0.25
6.3.1946	29		1.86	0.12	0.62	0.19	2.79	—	0.93	1.96	2.89	−1.00
13.4.1946	34		1.34	Nil	0.70	0.19	2.23	11.0	0.64	2.15	2.79	−0.56
27.1.1945	21	47	1.72	Nil	0.66	0.29	2.67	11.5	0.81	1.78	2.59	+0.08
12.3.1945	27		2.04	Nil	0.52	0.19	2.75	10.8	0.58	3.00	3.58	−0.83
23.4.1945	33		2.32	0.20	0.77	0.19	3.48	11.0	0.76	1.80	2.56	+0.92
28.5.1945	38		2.00	Nil	0.45	0.19	2.64	11.0	0.81	2.00	2.81	−0.17
9.2.1945	8	48	0.81	0.40	0.90	0.19	2.30	10.9	0.70	1.71	2.41	−0.11
23.3.1945	14		2.05	0.42	0.67	0.19	3.33	11.4	0.80	3.56	4.36	−1.03
8.5.1945	20		1.87	0.36	0.51	0.19	2.93	10.2	0.52	3.65	4.17	−1.24
16.6.1945	26		2.40	0.29	0.54	0.19	3.42	10.2	0.63	2.55	3.18	+0.24
1.8.1945	32		2.01	0.27	0.57	0.19	3.04	10.2	0.36	1.73	2.09	+0.95
3.9.1945	38		1.20	0.40	0.52	0.19	2.31	10.6	0.96	1.46	2.42	−0.11
21.6.1945	16	49	1.46	Nil	0.45	Nil	1.91	10.8	0.66	1.22	1.88	+0.13
11.8.1945	24		1.12	Nil	0.43	Nil	1.55	10.0	0.77	1.12	1.89	−0.34
21.9.1945	30		0.99	0.27	0.41	Nil	1.67	10.4	1.06	0.83	1.89	−0.22
3.11.1945	36		1.33	0.12	0.28	Nil	1.73	10.6	0.77	1.21	1.98	−0.25
21.7.1945	27	50	1.32	Nil	0.55	Nil	1.87	10.8	0.83	0.82	1.65	+0.22
4.9.1945	33		1.02	0.27	0.46	Nil	1.75	9.9	0.62	1.04	1.66	+0.09
2.10.1945	39		1.16	Nil	0.34	Nil	1.50	8.9	0.92	1.35	2.27	−0.77
14.12.1945	14	51	1.57	0.27	0.60	Nil	2.44	10.0	1.01	2.20	3.21	−0.77
12.2.1946	22		1.12	0.56	0.56	Nil	2.24	10.0	0.76	1.29	2.05	+0.19
18.3.1946	27		1.30	0.49	0.60	Nil	2.39	10.0	0.48	0.45	0.93	+1.46
7.5.1946	34		1.88	0.44	1.60	Nil	3.92	10.0	0.83	1.79	2.62	+1.30
6.6.1946	38		1.84	Nil	0.74	Nil	2.58	10.0	0.78	2.90	3.68	−1.10
8.1.1946	8	52	0.83	0.73	0.64	0.19	2.39	10.5	0.24	2.28	2.52	−1.13
22.2.1946	14		0.86	0.40	0.83	0.19	2.28	9.8	0.71	2.12	2.83	−0.55
24.4.1946	22		2.43	0.45	0.92	0.19	3.99	10.0	0.55	3.60	4.15	−0.16
4.6.1946	28		1.66	0.20	0.53	0.19	2.58	10.0	0.64	3.30	3.94	−1.36
8.7.1946	33		1.06	0.49	0.31	0.19	2.05	—	0.57	3.06	3.63	−1.58
6.8.1946	37		1.42	0.25	0.45	0.19	2.31	10.8	0.45	1.84	2.29	+0.02
5.3.1946	14	53	1.75	0.97	0.44	Nil	3.16	9.9	0.99	5.40	6.39	−3.23
16.4.1946	20		1.92	0.40	0.50	Nil	2.82	9.3	0.75	3.20	3.95	−1.13
28.5.1946	28		1.29	0.32	0.39	Nil	2.00	11.0	0.65	2.40	3.05	−1.05
16.7.1946	35		1.26	0.44	0.42	Nil	2.12	9.9	0.74	2.25	2.99	−0.87

TABLE II.

Calcium Balances.

	Group I	Group II	Group III	Group IV
Number of balances	84	36	44	63
Percentage negative balances	80	44	22.5	54
Percentage equilibrium	7	3	4.5	27
Percentage positive balances	13	53	73	19

more than a week, as their supplies had run out, owing to a miscalculation. The 63 balances analyzed in Group IV represent all the figures given in Section 2 of Table I. It was considered desirable to lump all these balances together, in spite of the varying dosage of Calciferol, to see whether a definite influence of Calciferol could be demonstrated.

Calciferol action, were the numbers sufficient to be statistically significant. This is hardly the case.

The figures in Table III are somewhat surprising, as the increase in the percentage of positive phosphorus balances in Group III was even more striking than the increase in positive calcium balances as

TABLE III.

Phosphorus Balances.

	Group I	Group II	Group III	Group IV
Number of balances	84	36	44	63
Percentage negative balances	40	42	16	41
Percentage equilibrium	12	11	7	21
Percentage positive balances	48	47	77	38

Group I—Controls.
Group II—Calcium phosphate.
Group III—Calcium phosphate plus Calciferol.
Group IV—Progressive doses of Calciferol only.

As the calcium intakes in Group I and Group IV cases were similar any marked increase in the percentage of Group IV positive balances, as compared with Group I, could be considered proof, or at any rate an indication, that Calciferol by itself does have a definite effect on calcium and phosphorus metabolism during pregnancy. There is, in fact, no statistically significant increase in the percentage of positive calcium balances, though there is a definite decrease in the percentage of negative balances. The increase in percentage of equilibria might be considered to reflect

shown in Table II. The Group IV figures show no decrease in the percentage of negative phosphorus balances, though there is an increase in the percentage of equilibria, parallel to the increase of calcium equilibria in Table II.

In an attempt to assess the influence of the Calciferol factor the balance figures taken from Section 2 of Table I were further analyzed out in relation to calcium intake levels, and are given in Table IV.

When these figures are compared with the corresponding figures (printed in brackets) from Table IV in a previous paper

TABLE IV.

Correlation between Calcium Intake Levels and Calcium Balances.
(Analysis of Group IV Cases—Calciferol only).

Intake per 24 hours	No. of balances	Balance positive	Equilibrium	Balance negative	Percentage negative balances
Below 1 g.	18 (27)	1 (?1)	4 (1)	13 (25)	60 (93)
Between 1.1–1.5 g.	37 (20)	3 (4)	1 (0)	4 (8)	50 (67)
Between 1.6–2.0 g.	8 (12)	8 (2)	12 (1)	17 (17)	46 (86)

the decrease in the percentage of negative calcium balances shown in Table II would seem to be of more definite significance. A corresponding comparison of the phosphorus balance figures, in relation to phosphorus intake, is given in Table V.

the Calciferol factor, the women in Group III (calcium phosphate plus Calciferol) were given much larger doses than is usual in clinical practice. They were given 18,000 units up to the end of the fifth month, 27,000 during sixth and

TABLE V.

Correlation between Phosphorus Intake Levels and Phosphorus Balances.
(Analysis of Group IV Cases—Calciferol only).

Intake per 48 hours	No. of balances	Balance positive	Equilibrium	Balance negative	Percentage negative balances
Below 2 g.	1 (2)	1 (1)	0 (1)	0 (0)	0 (0)
Between 2.1–2.5 g.	3 (13)	1 (1)	1 (1)	1 (11)	33 (84)
Between 2.6–3.0 g.	16 (11)	5 (4)	2 (4)	9 (3)	56 (36)
Between 3.1–3.5 g.	19 (15)	7 (11)	5 (0)	7 (4)	37 (27)
Between 3.6–4.0 g.	15 (17)	6 (7)	4 (2)	5 (8)	33 (46)
Between 4.1–4.5 g.	5 (12)	4 (7)	0 (2)	1 (3)	20 (40)
Between 4.6–5.0 g.	3 (5)	1 (3)	1 (0)	1 (2)	33 (40)
Over 5 g.	1 (4)	0 (3)	0 (1)	1 (0)	100 (0)

These figures are more difficult to interpret, though it would seem (after eliminating the extreme upper and lower limits of intake, covering a number of balances so small as to be statistically negligible) that a 48-hour intake of not less than 3 g. of phosphorus represents the minimum safety level.

OPTIMUM CALCIFEROL DOSAGE.

As was pointed out in a previous paper (Obermer, 1946b) dealing with

seventh months and then 36,000—the same dosage as cases 51 to 53 in the present paper. Although the results were significant, as is shown by the figures given in Table II, it was considered possible that smaller doses—in conjunction with calcium phosphate supplements—would have given just as good results. In planning the ascending scale of dosage in these Group IV cases, therefore, it was hoped that the results might point to an optimal zone of dosage.

A closer analysis of the figures in Section 2 of Table I, with this end in view, did not yield conclusive results. A comparison was made between the ratio of P in urine/P in faeces, calculated on the phosphorus intake and output figures, parallel to the calcium figures given in Sections 1 and 2 of Table I. It was difficult, if not impossible, to attach any importance to variations in this ratio. It is possible that the full figures for this ratio, covering the balances in the whole series of cases, and which will be given in the final report, may show some significant alteration in this ratio in Group III and Group IV cases as opposed to those who were not given Calciferol. Theoretically some such change should be found, if the action of Calciferol on human beings is at all similar to the action which has been experimentally observed in dogs (Shimotori and Morgan, 1943). However, from the series of balances determined on the cases discussed in this paper—admittedly too limited in number—we are not entitled to draw any dogmatic conclusions either as to the optimum dosage of Calciferol or as to the mechanism of Calciferol action. Taking the Group III and Group IV cases together, however, it is possible to make a provisional deduction:

That a dosage of less than 9,000 units in the first half of pregnancy and 18,000 units in the latter half does not show any definite evidence of an effective influence on either the calcium or phosphorus balances.

ANALYSIS OF CASES 37 TO 53.

The balance figures mentioned below will be found by referring to Section 1 of Table I for "control" investigations and to Section 2 of Table I for investigations carried out during periods when the cases were ingesting supplements of Calciferol.

CASE 37. Age 25; primipara. Height, 160 cm.; weight, 51 kg. Investigated 4 times. There were 2 control balances—at the 18th and 30th weeks; and 2 Calciferol balances—at the 24th and 36th weeks. All show positive calcium balances, except on the last occasion, in spite of very low calcium intakes (average of less than 1.1 g. per 24 hours). This case had very small stools throughout. This apparently was her habit at all times and though some of the stools were hard and faceted she suffered no discomfort.

Temperament. Exceptionally cheerful and well balanced—no worries.

Influence of Calciferol. No evidence that the 800 units per day in the Government capsule had any effect whatsoever.

CASE 38. Age 22; primipara. Height, 170 cm.; weight, 72 kg. Investigated 3 times. No control balance as she took a Government capsule per day throughout pregnancy. One positive balance and 2 equilibria, in spite of a calcium intake which averaged 1.2 g. per day.

Temperament. Stupid and placid.

Influence of Calciferol. No definite evidence.

CASE 39. Age 23; primipara. Height, 155 cm.; weight, 64.5 kg. Investigated 4 times. First control balance at 24th week; extremely low calcium intake. Heavy negative balance. The same applies to the first Calciferol balance (1,000 units per day) at the 31st week. Shortly after this investigation, during a routine examination at the antenatal clinic, her arterial pressure was found to be higher than was considered normal and she was put to bed. She had no abnormal symptoms and felt perfectly well, but as the pressure did not fall she was taken into the lying-in hospital at Brocket Hall at about the 36th week of her pregnancy. There she was dieted as well as rested. The "control" figures for the 38th week were collected when she was in bed there, though back on normal diet. She had not been taking her Calciferol supplement while in hospital. A negative balance will be noted. She was then put back on a daily dose of 2,000 units for the 15 days prior to the last Calciferol balance at the 40th week. On a calcium intake, which was practically identical to the intake at the 38th week, the balance had become positive.

Temperament. Cheerful and equable.

Influence of Calciferol. It is possible that as little as 2,000 units per day did, in fact, have a definite effect, in view of her temperament and the conditions of complete tranquility—she was a little bored but quite happy and cheerful.

CASE 40. Age 30; primipara. Height, 174 cm.; Weight, 77 kg. Investigated 4 times. The control balance at the 14th week was positive, though the phosphorus balance was negative. At the 20th week (1,000 units) and at the 26th and 31st weeks (2,000 units) the balances were negative.

Temperament. Over-conscientious—did far too much—no tranquility of mind.

Influence of Calciferol. No evidence.

CASE 41. Age 27, second pregnancy. Height, 171 cm.; weight, 60.5 kg. (Previous normal pregnancy and labour in 1944.) Investigated 4 times. Heavy negative control balance and negative balances at 15th week (1,000 units) and 27th week (2,000 units), equilibrium at the 21st week (1,000 units).

Temperament. Dissatisfied, always whining, incompetent, worried about trifles.

Influence of Calciferol. No evidence.

CASE 42. Age 23; primiparae. Height, 159 cm.; weight, 53 kg. Investigated 4 times. Exceptionally small control intake at 12th week (less than 0.6 g. per day). Heavy negative balance. At 18th week (3,000 units) positive balance, at 24th week (3,000 units) and 31st week (6,000 units) equilibria in spite of a consistently inadequate intake. The stools in this case were definitely " constipated " though no discomfort was experienced.

Temperament. Lethargic—never seemed to read or take an intelligent interest in anything—sat about ruminating.

Influence of Calciferol. It is probable that the relatively small doses of 3,000 and 6,000 units respectively did exert some influence in this case. It is difficult to avoid postulating that a given dosage of Calciferol exerts an influence in direct inverse proportion to the nervous excitability of the subject.

CASE 43. Age 33; second pregnancy. Height, 167 cm.; weight, 74.5 kg. (Previous pregnancy in 1944. Toxaemia, labour in April, 1944; 6 weeks

premature, baby only lived 27 hours and died of convulsions.) Investigated 5 times. Control balance at 9th week—negative. At 15th and 21st weeks (3,000 units) negative balances. Equilibrium at 28th week and negative at 34th week (6,000 units on both occasions).

Temperament. Active, cheerful and well-balanced, but frightened of recurrence of foetal death and somewhat worried about inability to find flat for herself and husband—living with parents.

Influence of Calciferol. The initial increase of dosage from 3,000 to 6,000 may have had some effect. As her temperament was favourable and her conditions unfavourable a somewhat larger dose, together with a calcium phosphate supplement, might have been effective.

CASE 44. Age 32; primipara. Height, 159 cm.; weight, 62 kg. Investigated 4 times. (Figures for the first 3 occasions only shown on Table I.) Control balance heavily negative. Balance at 21st week (3,000 units) also negative. Balance at 28th week (6,000 units), positive. This case was again investigated at the 34th week. The figures have not been included, as she had been given a supplement of calcium phosphate by a new doctor at the antenatal clinic. The figures on this 4th occasion show a negative balance of 0.5 g. calcium, in spite of a calcium intake of 4.57 g. and a Calciferol dosage of 9,000 units.

Temperament. "Always been very highly strung, doctor"; "nervous breakdown", February 1945. Fussed and worried throughout her pregnancy.

Influence of Calciferol. Doubtful.

CASE 45. Age 28; primipara. Height, 172 cm.; weight, 57 kg. Investigated 5 times. All balances heavily negative, in spite of a dosage of 3,000 units at the 15th week, 6,000 units at the 22nd and 28th weeks and 9,000 units at the 34th week.

Temperament. Pleasant woman but general physical condition poor—housing conditions very bad—generally harried—much worried about husband.

Influence of Calciferol. No evidence.

CASE 46. Age 25, primipara. Height, 155 cm.; weight, 54 kg. Investigated 5 times. No control balance as she was taking a Government capsule throughout her pregnancy, as well as the Calciferol supplement. At the 11th week (800 units)

balance was positive, probably because she passed unusually small stools. The balance at the 17th and 23rd weeks (3,800 units), the 29th week (8,800 units) and the 34th week (9,800 units) were all negative.

Temperament. "Highly strung"—very upset by bombing; bad housing conditions; unhappy and dissatisfied.

Influence of Calciferol. No evidence.

CASE 47. Age 27; primipara. Height, 162 cm.; weight, 49.5 kg. Investigated 5 times. Control balance negative. Equilibrium at the 21st week (9,800 units). Negative balance at the 27th week (9,800 units), positive balance at the 33rd week (9,800 units) and equilibrium at the 38th week (18,800 units).

Temperament. Equable; cheerful; exceptionally good sense of humour. This patient was subjected to both flying bombs and rockets during the first two-thirds of her pregnancy but they did not seem to worry her.

Influence of Calciferol. It is probable that the larger doses had a definite effect.

CASE 48. Age 26, primipara. Height, 158 cm.; weight 63.5 kg. Investigated 6 times. No control balance as she was taking a Government capsule as well as the Calciferol supplement throughout pregnancy. Equilibrium at 8th week (8,000 units). Negative balance at 14th and 20th weeks (9,800 units), positive balances at 26th (9,800 units) and 32nd week (18,800 units), equilibrium at the 38th week (27,800 units).

Temperament. Florid; cheerful; energetic; always optimistic, never worried.

Influence of Calciferol. It is probable that the higher dosage (18,000 units and over) had a definite effect. It should be noted that the calcium intake figures for this case were higher than the average in this series (up to 1.79 g. per day).

CASE 49. Age 31, primipara. Height, 162 cm.; weight 62 kg. Investigated 5 times. Control balance heavily negative. Balance at 16th week (9,000 units) equilibrium and slightly negative at the 24th and 30th weeks (18,000 units) and 36th week (27,000 units).

Temperament. "Worried". Mother had nearly

died of severe nephritis in pregnancy. She was frightened that she would follow suit.

Influence of Calciferol. As the calcium intake figures were consistently below 1.0 g. per day it is probable that the Calciferol exerted a definite influence.

CASE 50. Age 22, primipara. Height, 172 cm.; weight 63 kg. Investigated 4 times. Control balance slightly negative. At 27th week (18,000 units) balance positive, at 33rd week (27,000 units) equilibrium, and negative balance at 39th week (27,000 units). On this last occasion it should be noted that the calcium intake was only 0.78 g. per day.

Temperament. Cheerful, intelligent and well balanced.

Influence of Calciferol. Highly probable. If her calcium intake had been doubled throughout, her balance figures might well have been optimal.

CASE 51. Age 32, primipara. Height, 158 cm.; weight 65.5 kg.

CASE 52. Age 23, primipara. Height 177 cm.; weight, 74 kg.

CASE 53. Age 33, primipara. Height, 168 cm.; weight 54 kg.

These 3 cases can be discussed together as their Calciferol dosage was identical. The predominance of positive balances in Case 51 contrasts strongly with the predominantly negative balances in Case 52, and still more with the persistently heavy negative balances of Case 53.

CASE 51. The perfect example of a human ruminant. Few, if any, interests outside food and bed. It will be noted that her balance figures progressively improved, on increasing dosage, up to the last investigation at the 38th week, when she had an exceptionally large stool and an inadequate intake.

CASE 52. An intelligent and well-balanced woman who was very worried throughout her pregnancy by the necessity for finding a house or flat near her husband's work.

CASE 53. An extremely unfortunate temperament. The sort of woman who always considered

herself the victim of a specially malign fate. When she became pregnant she hesitated a long time before deciding to continue with it—was not in love with her husband and, throughout pregnancy, tortured herself with doubts as to the advisability of having a child and the consequences that would ensue.

Control balance at the 8th week was not representative, as only one small stool was passed and the figures had to be multiplied by 2 to arrive at an approximate balance. All the other investigations show a markedly negative balance.

Influence of Calciferol. As the calcium intake in these 3 cases was, roughly, similar (all below our " safety " level) and the diets of all 3 women more varied and abundant than the average for this series, it may be legitimate to assume that the dosage of Calciferol was adequate in Case 51— optimum temperament, tranquil life during pregnancy; less adequate in Case 52—favourable temperament, absence of tranquility during pregnancy; and totally inadequate in Case 53—unfavourable temperament, worry and anxiety during pregnancy.

THE TEMPERAMENTAL AND EMOTIONAL FACTORS.

All general practitioners with an extensive obstetric practice and practising obstetricians know that these factors are of great importance. It would be of great value, however, to be able to prove this fact in a quantitatively experimental manner. Unfortunately, however, it is extraordinarily difficult to bring forward statistical proof. On the other hand it is difficult to find any other explanation for (a) the significant proportion of negative balances found, in the cases of this series, who were given both adequate supplements of calcium phosphate and very high doses of Calciferol, that is, 22.5 per cent negative balances shown on Table II for Group III, and (b) the variable reaction of different Group IV cases to identical doses of Calciferol.

THE TEMPERAMENTAL FACTOR.

It is logical to assume that the differences in endocrine tempo and autonomic balance, which underly temperament, influence the metabolic rhythm as a whole. Of recent years much work has been done on the influence of hormones and functional endocrine variations on metabolism. The reader is referred to Holmes (1945) for a general survey. A few references to the influence of the parathyroid (Albright, *et al.*, 1929; Ellsworth, 1932; Cantarow, Brundage and Housel, 1937), the pituitary (Bauer and Aub, 1941; Pugsley and Anderson, 1934; Schriver and Bryan, 1935), the thyroid (Althausen, Kerr and Stockholm, 1939; 1941; Johnston, 1941a), and the ovaries (Johnston, 1941b; Albright, Smith and Richardson, 1941) will be sufficient to give the reader a bird's-eye view of the work on this fascinating and complex subject. Further, the metabolic studies which have been carried out on all the cases in this series, and which will be published later, show that the degree of metabolic fluctuation is at least equal to one's clinical appreciation of temperamental variations.

THE EMOTIONAL FACTOR.

It is a commonplace that anxiety and worry exert a profound influence on metabolism. The interpretation of the figures and statistics, which have been given in this paper, must needs be influenced by this factor. Anxiety has already been stressed by other workers in pre-war days (Macy, *et al.*, 1930). The degree of anxiety to which persistent bombing gave rise, in the cases of this series, from the beginning of the experiment in 1943 up to the end of the war in Europe in May 1945, can hardly be overestimated. It is known that the female pregnant organism is more labile than the non-pregnant one. A quantitative reflection of the effect of this factor is shown by

the fact that over 80 per cent of the urines passed by the cases investigated during the bombing periods contained quantities of glucose sufficiently large to be susceptible of measurement by delicate methods, in many cases much larger quantities. Very few urines passed by the cases investigated since May 1945 have contained appreciable quantities of a reducing substance. When considering the figures in Tables II, III, IV and V it should be remembered that Group IV cases—Cases 37 to 53—considered in this paper were, with one exception, investigated in the post-war period. It may well be, therefore, that the decreased number of negative balances in Group IV could partly, or even wholly, be accounted for by less anxiety, and might be only partly or, perhaps not at all, attributable to Calciferol.

This is only another example of the complexity of the subject of mineral metabolism. So many intrinsic and extrinsic factors are to be considered in each case that rash interpretations and generalizations needs must be invidious.

What is the Clinical Significance of Negative Calcium Balances?

To some, the fact that 80 per cent of the cases in this series who had no calcium or Calciferol supplements (controls—Table II) showed a negative calcium balance will seem a startling finding. On the other hand these cases are drawn from the labouring and middle classes—the overwhelming majority of the population. The author's experience, based on the metabolic investigation of some hundreds of pregnant women throughout pregnancy during the last 20 years, leads him to believe that these figures are representative. Can such a common phenomenon be considered pathological? On the one hand we have learnt to believe in the extraordinary powers of adaptation of the human organism to adverse circumstances. On the other hand we know that the foetal requirements for calcium during pregnancy (Mitchell and Curzon, 1939), exclusive of that of the maternal organism, are roughly 25, 50, 84, 125, 175, 234, and 300 mg. daily, respectively, for the last 7 lunar months. In theory, therefore, these persistently negative balances must result in some damage to the maternal organism and, in some cases, even to that of the foetus. It is to be hoped that the labour details as well as the maternal and foetal postnatal reports on the cases in this series, which will be published later, may throw some light on this important subject. It is imperative, also, that further studies of this nature and in larger numbers be carried out on normal pregnant women. These studies must be even more comprehensive and include a reliable method for assessing appreciable degrees of decalcification of the maternal skeleton, such as that of Mack *et al.* (1931). A statistically significant number of cases should, also, be included on adequate calcium phosphate supplements and given ascending doses of Calciferol. It should thus be possible to establish an optimum Calciferol dosage or, rather, a "safety" level for different temperaments and conditions of pregnancy. The findings of such a series would either bear out or contradict, with authority, the tentative conclusions to which the writer has been led by the figures derived from this preliminary experiment.

Practical Conclusions.

On the basis of the figures given in this and the two previous papers, which cover 227 forty-eight hour investigations, at different phases of pregnancy, the following tentative conclusions have been arrived at:

(1) That the phosphorus intake of

normal pregnant women on a generous all-round diet is usually adequate. When the diet is insufficient owing to poverty or any other reason, and we suspect that the daily intake of P is less than 1.5 g. per day, a supplement of phosphorus should be given.

(2) That the minimum "safety" levels of daily calcium intake are 2 g. of Ca element from the beginning of pregnancy to the end of the 7th month and 2.5 g. from the 8th month to term. These amounts cannot be arrived at without a supplement, however generous and all-round the diet. A pregnant woman who consumes her statutory pint of milk per day (0.72 g. Ca.) together with her daily ration of cheese (0.08 g. Ca) and a high average of "other foods" intake (0.30 g. Ca) arrives at a total 24-hour intake of only 1.1 g. To ensure adequate reserves every pregnant woman should be given a supplement of calcium phosphate, containing at least the following amounts of calcium and phosphorus elements:

	Ca	P
3rd to 5th months	0.64 g.	0.282 g.
6th to 8th months	0.95 g.	0.423 g.
8th month to term	1.26 g.	0.564 g.

(3) In the climatic conditions of Great Britain every pregnant woman also requires a supplement of Calciferol. The dosage should be varied according to her temperament and the emotional stresses and strains to which she is subjected during her pregnancy. 6,000 units during the first 6 months and 12,000 units during the last 3 months may be adequate for an exceptionally placid woman in conditions of tranquility. The dose for the average woman in average conditions should probably be not less than 10,000 units in the first 6 months and 20,000 during the last 3 months. Even these doses should be increased under favourable circumstances, playing on an unfavourable temperament.

(4) Small stools are desirable and even "constipation" should be tolerated, if it gives rise to no discomfort or mechanical trauma.

(5) Laxatives and drastic purgatives should be abstained from. Under exceptional circumstances small doses of paraffin or an agar preparation should be resorted to.

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Studies in Prematurity, Stillbirth and Neonatal Death

Part II. Delivery and its Hazards.

BY

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Introduction.

In this series of studies a statistical analysis has been made of 7,599 births occurring in the Simpson Memorial Pavilion, Edinburgh during the 3-year period, 1942, to 1945 inclusive, in order to evaluate the principal aetiological factors influencing the incidence of prematurity, infant death and stillbirth.

As was pointed out in Part I (Drillien, 1947), a large number of similar surveys, with widely divergent conclusions, have been carried out during the past 15 years in America and elsewhere, and it was suggested that the main reasons for these discrepancies consist of the absence of adequate controls, failure to differentiate between emergency and booked cases, frequent omission of stillbirths when considering infant wastage, and the adoption of varying criteria of prematurity and viability. In the analysis of this series, a special code card was designed, on which were entered details from the infant and obstetric records of every premature birth, stillbirth and infant death occurring during the period, with a 1 in 10 sample, to act as a control group, of mature infants born in hospital and surviving their discharge.

The previous paper dealt with prematurity-rates and showed how closely outcome—whether the infant was stillborn, died or survived—was related to birth-weight. The factors affecting birth-weight were then considered under 4 headings, complications of pregnancy, age of mother, legitimacy and sex of infant. This present paper deals with delivery and its hazards and Part III with deaths and stillbirths.

Modes of Delivery in Primiparae and Multiparae.

In Table I the distribution of modes of delivery is compared for booked and unbooked cases both for multiparae and primiparae, multiple births being excluded. The rates for the booked primiparae give the nearest approach to what would be expected in a random sample of first births in the general population. Comparing the rates for primiparae and multiparae the most striking feature is seen to be the excess of instrumental delivery among the former. In both booked and unbooked groups the rate is over 3 times that of the multiparae. In Table II the mode of delivery is compared in booked cases for premature and mature infants. Instrumental delivery is seen to be the more common for mature infants, and Caesarean section for the premature group.

Outcome According to Mode of Delivery.

Table III gives the outcome in the different modes of delivery for booked cases,

excluding multiple births. Unbooked cases have not been included, as their outcome is so largely determined by the complications of pregnancy for which the majority of emergency cases are admitted. There is a very great excess of deaths and stillbirths in breech deliveries and Caesarean section, and a smaller excess of stillbirths in cases of instrumental delivery. Table IV shows the wastage rates for different modes of delivery according to whether the infant was premature or mature. In each group the difference is also shown between wastage

3. There is an increased risk in Caesarean section for both premature and mature infants, especially the latter.

The excess wastage in breech delivery and Caesarean section may be due to:

1. Dangers inherent in the method of delivery itself.

2. Complications incident to or accompanying the method of delivery. The information relating to these 2 methods of delivery were therefore further investigated with special reference to these possible alternatives.

TABLE I.

Mode of Delivery, Excluding Multiple Births.

Mode of delivery	Primiparae		Multiparae	
	Booked per cent	Unbooked per cent	Booked per cent	Unbooked per cent
1. Vertex, spontaneous	80.4	48.5	87.1	69.4
2. Vertex, low forceps	8.0	8.1	1.3	1.5
3. Vertex, mid or high forceps	2.3	14.1	1.9	2.9
4. Version and extraction	5.5	6.1	1.3	4.8
5. Breech, assisted or spontaneous ..	2.2	6.5	2.9	10.8
6. Caesarean section	1.4	14.8	5.3	8.2
7. Craniotomy and other mutilating operations	0.1	1.8	0.1	2.3
Total	100.0	100.0	100.0	100.0
Number of cases	4249	446	1647	729

by each mode of delivery and that observed in cases of spontaneous vertex delivery. The rate for version and extraction is based on only 3 cases, and reliance cannot be placed upon it. The table suggests the following conclusions:

1. Instrumental delivery appears to be as safe as spontaneous vertex for premature infants though it carries an increased risk in the mature.

2. Breech delivery has a considerably greater wastage-rate˙ than any other method in both premature and mature births.

Breech Delivery.

Breech delivery is commonly considered to be favoured by anything which prevents the head from engaging in the pelvic brim, such as placenta praevia or hydramnios. The dangerous complication of prolapse of the cord also occurs with increased frequency in breech presentation. These complications all carry a heavy mortality-rate. Table V gives the survival-rates in all breech deliveries, excluding cases of hydramnios, placenta praevia and prolapsed cord, and in spontaneous˙vertex deliveries excluding the same 3 complica-

TABLE II.

Mode of Delivery in Booked Cases, Excluding Multiple Births

	Primiparae		Multiparae	
Mode of delivery	Premature per cent	Mature per cent	Premature per cent	Mature per cent
1. Vertex, spontaneous	80.3	80.5	76.4	88.1
2. Vertex, low forceps	2.8	8.3	1.4	1.3
3. Vertex, mid or high forceps	0.8	2.4	0.7	2.1
4. Version and extraction	1.6	5.8	0.0	1.4
5. Breech, assisted or spontaneous ...	8.7	1.8	10.0	2.3
6. Caesarean section	5.5	1.2	11.4	4.7
7. Craniotomy and other mutilating operations	0.4	0.1	0.0	0.1
Total	100.0	100.0	100.0	100.0

TABLE III.

Outcome by Mode of Delivery in Booked Cases, Single Births

	Primiparae			Multiparae		
Mode of delivery	Per cent lived	Per cent died	Per cent stillborn	Per cent lived	Per cent died	Per cent stillborn
Vertex, spontaneous	96.9	1.2	2.0	95.1	1.7	3.2
Vertex, low forceps	96.2	1.5	2.4	95.4	0.0	4.5
Vertex, mid or high forceps	93.8	1.0	5.2	93.8	3.1	3.1
Version and contraction	95.3	0.9	3.8	95.2	0.0	4.8
Breech	75.5	10.6	13.8	74.9	10.4	14.6
Caesarean section	81.7	10.0	8.3	91.9	5.7	2.3
Craniotomy, etc.			100.0			100.0

TABLE IV.

Percentage Wastage (Dead + Stillborn) by Mode of Delivery, Compared with Spontaneous Vertex, All Booked Single Births.

	Premature		Mature	
Mode of delivery	Wastage per cent	Difference from spontaneous vertex	Wastage per cent	Difference from spontaneous vertex
Vertex, spontaneous	33.8	—	1.6	—
Vertex, all forceps	33.3	− 0.5	3.8	+ 2.1
Version and extraction	25.0	− 8.8	4.4	+ 2.8
Breech	52.8	+19.0	15.1	+13.5
Caesarean section	36.7	+ 2.9	6.0	+ 4.4

tions. Even when the dangerous complications commonly occurring with breech delivery are excluded, there still seems to be a definite risk to the foetus, which is greater for mature than for premature infants. Here the survival-rate is 17.6 per cent less than in spontaneous vertex delivery, a difference which is statistically

1. Contracted pelvis. Either controlled trial labour or elective Caesarean section.

2. Emergency cases of contracted pelvis, admitted after prolonged labour, or with uterine inertia, or following failed forceps outside.

3. Local disease of uterus, such as fibroids, or of ovaries, such as cysts or

TABLE V.

Comparison of Survival Rates in Spontaneous Vertex and Breech Deliveries. All Single Births.

	Per cent survivors	Difference from spontaneous vertex	Standard deviation of difference	t
Premature:				
Vertex, spontaneous	61.5			
Breech (all)	39.2	−22.3	6.53	3.4
Breech (excluding complications)	48.0	−13.5	7.77	1.7
Mature:				
Vertex, spontaneous	100.0			
Breech (all)	79.5	−20.5	4.36	4.7
Breech (excluding complications)	82.4	−17.6	3.87	4.5

TABLE VI.

Indications for Caesarean Section. All Single Births.

	Premature	Mature	Total
1. Contracted pelvis, elective	4	84	88
2. Contracted pelvis, emergency	0	44	44
3. Local disease, elective	4	11	15
4. Chronic maternal disease, elective	5	10	15
5. Severe toxaemia, emergency	27	40	67
6. Placenta praevia, emergency	17	15	32
7. Following ruptured uterus, emergency... ...	0	2	2
8. Others, emergency	0	10	10
Total	57	216	273

highly significant. The next paper in this series will show the importance of asphyxia and intracranial haemorrhage in deaths and stillbirths occurring with breech delivery.

Caesarean Section.

Cases delivered by Caesarean section fall into the following categories:

other new growths. Elective Caesarean section.

4. Chronic maternal disease, such as cardiac disease, diabetes, chronic nephritis. Elective Caesarean section.

5. Severe toxaemias. Emergency cases, often admitted with some other complicating factor, chronic co-existent maternal

disease, bad obstetric history, or occurrence in an elderly primipara.

6. Placenta praevia, emergency cases.

7. Following ruptured uterus, emergency cases.

8. Other causes.

The numbers in each of these 8 categories are shown in Table VI. The next table gives the survival-rates for premature

Caesarean section seems to be a rather safer method of delivery than a spontaneous vertex, but the difference, being less than its standard deviation, is quite insignificant. The only significant difference is in the mature group, where emergency Caesarean sections seem to carry a definite risk as compared with spontaneous vertex delivery.

TABLE VII.

Comparison of Survival Rates in Spontaneous Vertex and Caesarean Section Deliveries. All Single Births.

	Per cent survivors	Difference from spontaneous vertex	Standard deviation of difference	t
Premature :				
Vertex, spontaneous	66.2	—		
Caesarean section, elective	76.9	+ 10.7	12.04	0.89
Caesarean section, emergency	59.1	− 7.1	7.95	0.89
Mature :				
Vertex, spontaneous	98.4	—		
Caesarean section, elective	95.2	− 3.2	2.49	1.29
Caesarean section, emergency	90.1	− 8.3	3.91	2.12

TABLE VIII.

Mode of Delivery by Maternal Age : Primiparae Except Multiple Births.

Mode of delivery	Mothers 15 to 24 per cent	Mothers 25 to 34 per cent	Mothers 35 to 44 per cent
Vertex, spontaneous	81.5	75.1	50.2
Vertex, forceps (low, mid and high)	7.5	15.8	20.9
Version and extraction	5.2	5.1	13.6
Breech	3.5	1.6	1.3
Caesarean section	2.2	2.1	13.2
Craniotomy, etc.	0.2	0.4	0.8
Total	100.0	100.0	100.0

and mature infants in cases of elective Caesarean section (categories 1, 3, and 4), emergency Caesarean section (categories 2, 5, 6, 7, and 8), and a control group of spontaneous vertex delivery in booked cases only.

In the premature group an elective

Comparison with Results of Other Workers.

In trying to compare these results with those in the literature, the same kind of difficulties were encountered as in the case of complications of pregnancy discussed in Part I. Here again the findings of different authors differed widely. In an analysis

of 17,728 deliveries at the Chicago Lying-in Hospital, Potter and Adair (1938) found the highest wastage-rate (deaths plus still-births) among infants delivered by version and extraction. The mortality was nearly twice as high as the next most dangerous group, breech delivery. Considering premature babies only, Dibble and Plass (1942) agree that version and extraction carries the greatest risk, though Clifford (1934a), also dealing with premature births, found the highest mortality occurred with breech delivery with Caesarean section a close second. Breese (1938) is of the opinion that the difference in mortality-rates between breech and vertex deliveries is accounted for by the fact that in the former case the babies were about 250 g. less in weight on the average, and that in Caesarean section there was no deleterious effect that could not be accounted for by birth-weight of the infant.

Mode of Delivery by Maternal Age.

Table VIII gives the distribution of modes of delivery of all primiparae, excluding multiple births, in 3 maternal age-groups, and the data are also shown in Fig. 1. The percentage of spontaneous vertex deliveries falls with increasing age, while the incidence of instrumental deliveries rises. Version and extraction, and Caesarean section rise sharply in the highest age group. Breech delivery is rather commoner in the youngest mothers. The figures for booked cases show the same general picture, though there is a slightly lower incidence of abnormal delivery in all age groups, and a correspondingly higher percentage of spontaneous vertex cases. The same information is shown in graphical form in Fig. 2 for premature and mature infants separately. Here spontaneous vertex deliveries are omitted and forceps and version and extraction are grouped together as " instrumental ". The figure

shows that the fall in the percentage of normal spontaneous deliveries with age is especially marked with mature infants, of whom less than half were so delivered in the oldest age group of mothers, amongst whom instrumental deliveries occurred in 39 per cent of the cases.
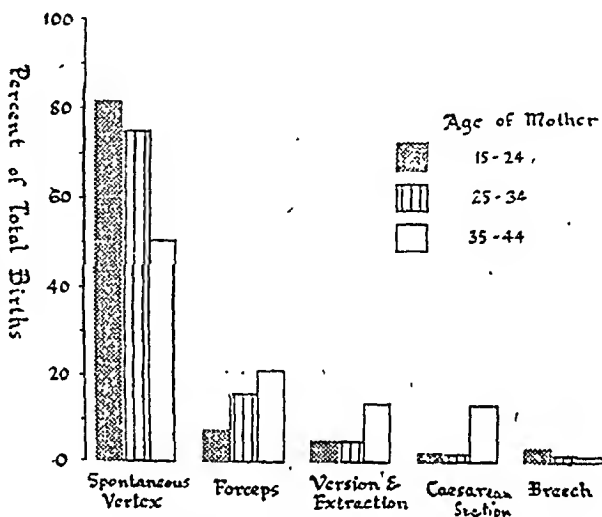

FIG. 1.

Mode of delivery in relation to age of mother.

Complications of Delivery.

The complications of delivery observed in this series of cases were as follows :

1. Prolapsed cord.

2. Malpresentation (e.g., brow, face, persistent occipito-posterior), including compound presentation.

3. Contracted pelvis.

4. Uterine inertia.

5. Deep transverse arrest.

6. Prolonged labour, not including cases already classified under 3, 4 and 5 above. Labour was taken to be abnormally prolonged when lasting more than 36 hours in primiparae and 24 hours in multiparae. It is realized that a better criterion would be the length of the second stage, but this information was frequently not available.
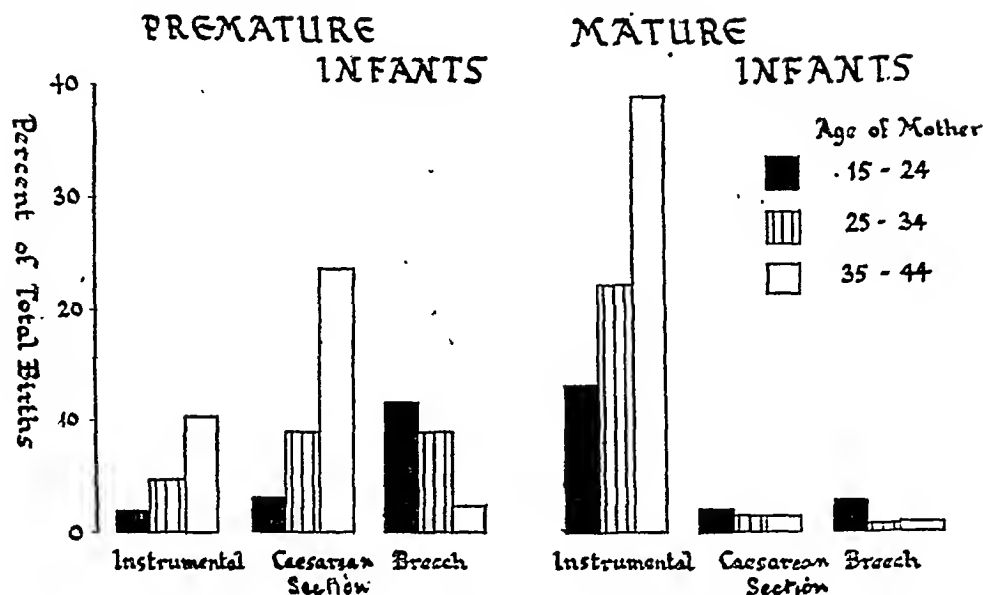
FIG. 2.

Mode of delivery in relation to age of mother and maturity of infant.

TABLE IX.

Incidence and Survival of Cases with Complications of Delivery: Booked Primiparae Except Multiple Births.

Complication of delivery	Number of cases	Premature incidence per cent	Mature incidence per cent	All babies incidence per cent	Survivors per cent
Prolapsed cord	19	1.1	0.4	0.4	36.1
Malpresentation	131	1.9	3.1	3.1	83.7
Contracted pelvis	58	1.1	1.4	1.4	88.1
Uterine inertia	45	0.4	1.1	1.0	90.0
Deep transverse arrest	108	0.8	2.6	2.5	92.3
Prolonged labour	144	3.8	3.3	3.3	87.9
Others	11	0.0	0.3	0.3	58.8
Total	516	9.1	12.2	12.0	

7. Others, including tonic uterine contractions, ruptured uterus, premature separation of placenta, and contraction ring.

Table IX shows the number and percentages of these complications occurring in booked primiparae, excluding multiple births, together with survival rates.

The complication of prolapsed cord is seen to carry a high mortality, only just over one third surviving. This may be due in part to the increased risk of other co-existent complications, such as placenta praevia, hydramnios, and congenital deformities, particularly anencephalus. The survival-rates for premature and mature infants was approximately the same, being 33.3 per cent and 37 per cent respectively.

c

Induction of Labour.

Surgical induction was performed on 264 patients with single pregnancies. No case was recorded as occurring with multiple births. The reasons for induction were as follows:

Toxaemias	146
including pre-eclamptic toxaemia	115
pre-eclamptic toxaemia + haemorrhage	10
eclampsia	16
Antepartum haemorrhage	62
Hydramnios	9
Intrauterine death	8
Nephritis	1
No cause given	38

Table X gives the percentage of inductions in primiparae in cases of toxaemia, placenta praevia, hydramnios, and all other cases. About one case in 11 of toxaemia had an induction, 1 in 7 of pla-

carry on the pregnancy as long as possible, with due regard, of course, to the mother's condition.

Clifford (1934b), in a paper describing a method for the determination of foetal size *in utero* has stressed the importance of delaying induction as long as possible as an aid to reducing the premature infant mortality. Barnes and Browne (1945), from an analysis of blood-pressures of nearly 2,000 nulliparous and parous women, came to the conclusion that toxaemia of pregnancy leaves of itself no permanent lesion and that there is therefore no justification for terminating a toxaemic prematurely in order to protect the mother from chronic hypertension. They point out, however, that the pregnancy may have to be interrupted if there

TABLE X.

Surgical Induction in Relation to Complications of Pregnancy:
All Primiparae Except Multiple Births.

	Number of cases	Number of surgical inductions	Per cent surgical inductions
Toxaemia	718	64	8.9
Placenta praevia	65	9	13.8
Hydramnios	26	5	19.2
All other cases of pregnancy	3883	17	0.4

centa praevia, 1 in 5 of hydramnios, and 1 in 250 of all other pregnancies. Table XI compares the percentage of infants under 3½ pounds and 5½ pounds in weight in induced pregnancies in primiparae, as compared with those allowed to go into labour without interference.

It has been shown in the previous paper (Part I) that an infant's chance of survival depends largely on its weight at birth, and also that toxaemia in the mother does not appear to have any adverse effect on the foetus apart from the effect on weight, as far as can be judged from survival-rates. It is therefore of the utmost importance to

seems to be a risk of eclampsia, or in the case of severe toxaemia to prevent death *in utero*. With regard to this last condition, there does seem to be a definite risk of a macerated foetus being associated with toxaemia, and this will be discussed more fully in Part III.

Table XI shows that surgical induction for toxaemia of pregnancy resulted in 8.3 per cent of the infants being less than 3½ pounds and 37.7 per cent less than 5½ pounds, these rates being more than 2½ times as high as in cases of toxaemia allowed to go into spontaneous labour; though of course it must be remembered

that the more serious cases will be selected for induction, and even if they were left alone these cases would be more likely to go into premature labour than those in which the toxaemia was less severe.

SUMMARY.

This paper comprises the second study in a series based on nearly 8,000 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive. In this part are considered different modes of delivery and their special hazards.

· A large excess of instrumental deliveries was found in first births. There was a marked excess of stillbirths and deaths in breech delivery and Caesarean section, and a smaller excess, of stillbirths only, in instrumental deliveries. For premature infants instrumental delivery appeared to carry no extra risk, but breech delivery was very dangerous.

Incidence of spontaneous vertex delivery falls markedly with increasing maternal age, while instrumental deliveries and Caesarean section rise. Breech delivery is slightly more common in young mothers.

Surgical induction was performed most commonly in cases of hydramnios, ante-partum haemorrhage and toxaemia. The proportion of very small babies in cases of induction was much greater than in cases going into labour without interference.

TABLE XI.

Percentages of Infants of Low Birth Weights in Induced and Non-induced Cases with Complications of pregnancy: All Primiparae Except Multiple Births.

	Infants below 3 pounds 9 ounces		Infants below 5 pounds 9 ounces	
Complication of pregnancy	Per cent of all non-induced cases	Per cent of all induced cases	Per cent of all non-induced cases	Per cent of all induced cases
Pre-eclamptic toxaemia	3.2	7.0	14.4	32.2
Eclampsia	5.8	6.3	19.3	37.6
Pre-eclamptic toxaemia with haemorrhage	6.3	10.0	31.3	70.0
All toxaemias	3.0	8.2	14.2	37.7
Antepartum haemorrhage	17.6	6.4	47.4	22.5
Hydramnios	20.5	88.9	38.7	88.9

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PART III. STILLBIRTHS AND NEONATAL DEATHS.

INTRODUCTION.

THIS paper forms Part III of a series of statistical studies into the aetiology of prematurity, infant death and stillbirth, based on 7,599 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive.

Data from infant and obstetric records of every stillbirth, neonatal death and premature birth occurring during the 3-year period were entered upon a specially weight, the principal factors affecting weight, and the special hazards of different modes of delivery. This paper deals with deaths and stillbirths.

DEATHS.

1. *Age at Death.*

The number of infant deaths recorded was 204, with the age distribution shown in Table I. There were 195 deaths within 28 days of birth; of the 9 that occurred after

TABLE I.
Age at Death, All Cases.

Age at death	Number of deaths	Per cent of deaths	Premature, per cent	Mature, per cent
0 to 6 hours	39	19.1	22.5	11.3
7 to 12 hours	20	9.8	13.4	1.6
13 to 24 hours	27	13.2	14.1	11.3
Total, 1st day	86	42.2	50.0	24.2
1st day	86	42.2	50.0	24.2
2nd day	34	16.7	14.1	22.6
3rd day	14	6.9	5.6	9.7
4th day	9	4.4	3.5	6.5
5th day	7	3.4	.2.8	4.8
6th day	10	4.9	4.9	4.8
7th day	5	2.5	1.4	4.8
Total, 1st week	165	80.9	82.4	77.4
1st week	165	80.9	82.4	77.4
2nd week	12	5.9	4.2	9.7
3rd week	15	7.4	7.1	8.1
4th week	3	1.5	1.5	1.6
Total, 1st month ...	195	95.6	95.1	96.1
After 1st month	9	4.4	4.9	3.9
Total	204	100.0	100.0	100.0

designed code card, together with data of a 1-in-10 sample of mature surviving infants, to act as a control group. The 2 previous parts (Drillien, 1947a; 1947b) dealt with prognosis according to birth- the first month 7 were premature babies, of whom 5 were below 3½ pounds in weight, and 2 suffered from gross congenital deformity which was the cause of death. The table shows that over 40 per cent of the

deaths took place on the first day, of which nearly half were in the first 6 hours. It is hard to draw the line between these very early deaths and stillbirths, as the aetiological factors affecting both are very similar. This emphasizes the importance of considering stillbirths as well as deaths when discussing infant wastage. The table also shows the percentage distribution by age of death of premature and mature infants, and these data are plotted as cumulative percentages in Fig. 1. Nearly a quarter of all the premature deaths took
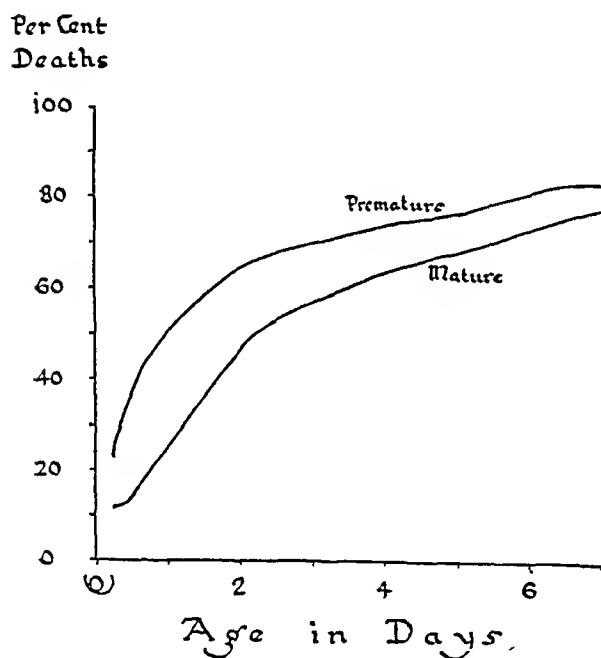
FIG. 1.
Cumulative curves of age at death.

place within 6 hours of birth, and one-half on the first day, these proportions being twice as high as those for mature infants. However good may be the care of premature babies, treatment after birth could have little effect in preventing these early deaths. Blackfan and Yaglou (1933) describe a routine of treatment for premature infants, but state that this was unable to

influence the death-rate, 80 per cent of the total occurring during the first 48 hours. Clifford (1934) relates how deaths after the first 48 hours were reduced over a period of 6 years after the establishment of air-conditioned nurseries and other measures, but he also found that the rate for the first 48 hours was unaffected.

2. *Causes of Death.*

The diagnosis of the cause of death in 173 of the cases was based on autopsy findings. In the remaining 31 cases the diagnosis was made as follows: Obvious congenital defect, 16. Deaths in premature infants, no other clinical findings, 12. Asphyxia diagnosed clinically, 1. Intracranial haemorrhage, diagnosed by lumbar puncture, 1. Gastro-enteritis, diagnosed clinically, 1.

Causes of death have been divided into the following main categories:

1. Erythroblastosis foetalis.
2. Gross congenital defect. In a number of cases the immediate cause of death' was infection, most commonly pneumonia.
3. Prematurity. This includes cases going to autopsy in which no pathological lesion could be detected apart from atelectasis, and in some cases a slight degree of subarachnoid and intraventricular haemorrhage. In a smaller number of cases autopsy was not performed, and no clinical diagnosis was made apart from prematurity.
4. Asphyxia. These cases showed subserous petechial haemorrhages, and often inhalation of liquor amnii and vernix, with or without commencing pneumonic changes. Intracranial haemorrhage was also found in a number of cases. Where subarachnoid or intraventricular haemorrhage occurred together with other signs of asphyxia; the haemorrhage was con-

sidered to be secondary to the asphyxia. In a smaller number of cases asphyxia was found together with a subdural haemorrhage. Here it is difficult to decide whether asphyxia or haemorrhage was the primary condition. These cases have been included under asphyxia.

5. Intracranial haemorrhage, subdural or intradural haemorrhage associated with birth trauma. In certain cases subdural haemorrhage occurred together with pneumonia. These cases have been included with pneumonia.

6. Pneumonia.

7. Meningitis.

8. Gastro-enteritis. Cases with a terminal pneumonia have been included in this group.

9. Congenital syphilis.

10. Others.

Table II gives causes of death in detail.

In Table III the causes of death are sub-classified by birth-weights. In the smallest infants prematurity alone accounts for nearly half the deaths, and with asphyxia and pneumonia included, for over 85 per cent of deaths. In the large premature babies, nearly one-third of the deaths are due to asphyxia and one-sixth to pneumonia, while congenital defects plus erythroblastosis account for a quarter of the deaths. In the mature group, congenital defects are by far the most important causes of death, accounting with erythroblastosis for about 55 per cent of fatalities. Section (c) of the table gives the death-rates per 1000 live births. This shows that in spite of the importance of congenital defects as a cause of death in mature infants their death-rate from this cause is a small fraction of that found among the premature. For all premature infants the death-rate from congenital defects is about 100 times that found for mature babies.

TABLE II.
Causes of Death.

1. Erythroblastosis	15	
Erythroblastosis plus meningitis ...	1	
		16
2. Congenital defects		41
3. Prematurity:		
No autopsy	12	
Autopsy, atelectasis only	12	
Autopsy, slight intracranial haemorrhage	15	
		39
4. Asphyxia	14	
Asphyxia plus sub-dural haemorrhage	6	
Asphyxia plus sub-arachnoid, intra-ventricular, or intracerebral haemorrhage	9	
Asphyxia plus pneumonic changes ...	11	
Asphyxia plus pneumonic changes plus intracranial haemorrhage ...	5	
		45
5. Subdural haemorrhage	7	
Subdural haemorrhage plus haemorrhagic disease	1	
		8
6. Pneumonia, unspecified	2	
Pneumonia, unspecified plus intracranial haemorrhage	3	
Pneumonia, post-asphyxial	4	
Pneumonia, post-asphyxial plus intracranial haemorrhage	2	
Bronchopneumonia	3	
Bronchopneumonia plus intracranial haemorrhage	4	
Bronchopneumonia plus thrush oesophagitis	1	
Septic inhalation pneumonia ...	3	
Septic inhalation pneumonia plus intracranial haemorrhage	3	
Septic staphylococcal pneumonia ...	4	
Septic staphylococcal pneumonia plus intracranial haemorrhage	2	
Septic staphylococcal pneumonia following skin infection	3	
		34
7. Meningitis, *B. coli*		2
8. Gastro-enteritis	9	
Gastro-enteritis plus pneumonia ...	2	
		11
9. Congenital syphilis		1
10. Other causes:		
Exsanguination	2	
Massive pulmonary haemorrhage ...	1	
Suprarenal haemorrhage	1	
Meconium peritonitis	1	
Gastric ulceration and haemorrhage	1	
Accidental asphyxia	1	
		7
Total		204

TABLE III.

Deaths by Birth-weights

(a) Number of deaths	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	5 pounds 9 ounces and over	All weights
1. Erythroblastosis	1	7	8	16
2. Congenital defects	5	10	26	41
3. Prematurity	33	6	0	39
4. Asphyxia	13	22	10	45
(4a. Asphyxia plus subdural haemorrhage)	(7)	(9)	(4)	(20)
5. Intracranial haemorrhage	0	4	4	8
6. Pneumonia	15	12	7	34
7. Meningitis	0	0	2	2
8. Gastro-enteritis	2	5	4	11
9. Congenital syphilis	0	1	0	1
10. Other causes	2	4	1	7
Total	71	71	62	204
(b) Percentages				
1. Erythroblastosis	1.4	9.9	12.9	7.8
2. Congenital defects	7.0	14.1	41.9	20.1
3. Prematurity	46.5	8.4	0.0	19.1
4. Asphyxia	18.3	31.0	16.1	22.1
5. Intracranial haemorrhage ...	0.0	5.6	6.5	3.9
6. Pneumonia	21.1	16.9	11.3	16.7
8. Gastro-enteritis	2.8	7.0	6.5	5.4
10. Other causes (including meningitis and congenital syphilis)	2.8	7.0	4.8	4.9
Total	100.0	100.0	100.0	100.0
(c) Rates per 1,000 births.				
1. Erythroblastosis	10	14	0.12	2.1
2. Congenital defects	51	19	0.39	5.4
3. Prematurity	333	12	0.00	5.1
4. Asphyxia	131	42	0.15	5.9
5. Intracranial haemorrhage ...	0	8	0.06	1.1
6. Pneumonia	152	23	0.11	4.5
8. Gastro-enteritis	20	10	0.06	1.5
10. Other causes (including meningitis and congenital syphilis)	20	10	0.05	1.3
Total	717	138	0.94	26.9

3. *Age at Death in Relation to cause of Death.*

Table IV shows that of all infants dying from prematurity or asphyxia, two-thirds died within the first 24 hours, and about 90 per cent within 3 days. Of those dying from congenital defects and erythroblastosis, 40 per cent lived longer than 3 days, and nearly 20 per cent survived for longer than 1 week. As would be expected, infections have a later age incidence. Nearly 40 per cent of all cases of pneumonia died after the first week, and all the fatal cases of gastro-enteritis survived their first week.

These figures further emphasize the comparatively minor role that treatment after

sidered to be secondary to the asphyxia. In a smaller number of cases asphyxia was found together with a subdural haemorrhage. Here it is difficult to decide whether asphyxia or haemorrhage was the primary condition. These cases have been included under asphyxia.

5. Intracranial haemorrhage, subdural or intradural haemorrhage associated with birth trauma. In certain cases subdural haemorrhage occurred together with pneumonia. These cases have been included with pneumonia.

6. Pneumonia.

7. Meningitis.

8. Gastro-enteritis. Cases with a terminal pneumonia have been included in this group.

9. Congenital syphilis.

10. Others.

Table II gives causes of death in detail.

In Table III the causes of death are sub-classified by birth-weights. In the smallest infants prematurity alone accounts for nearly half the deaths, and with asphyxia and pneumonia included, for over 85 per cent of deaths. In the large premature babies, nearly one-third of the deaths are due to asphyxia and one-sixth to pneumonia, while congenital defects plus erythroblastosis account for a quarter of the deaths. In the mature group, congenital defects are by far the most important causes of death, accounting with erythroblastosis for about 55 per cent of fatalities. Section (c) of the table gives the death-rates per 1000 live births. This shows that in spite of the importance of congenital defects as a cause of death in mature infants their death-rate from this cause is a small fraction of that found among the premature. For all premature infants the death-rate from congenital defects is about 100 times that found for mature babies.

TABLE II.

Causes of Death.

1. Erythroblastosis	15
Erythroblastosis plus meningitis ...	1
	16
2. Congenital defects	41
3. Prematurity:	
No autopsy	12
Autopsy, atelectasis only	12
Autopsy, slight intracranial haemorrhage	15
	39
4. Asphyxia	14
Asphyxia plus sub-dural haemorrhage	6
Asphyxia plus sub-arachnoid, intraventricular, or intracerebral haemorrhage	9
Asphyxia plus pneumonic changes ...	11
Asphyxia plus pneumonic changes plus intracranial haemorrhage ...	5
	45
5. Subdural haemorrhage	7
Subdural haemorrhage plus haemorrhagic disease	1
	8
6. Pneumonia, unspecified	2
Pneumonia, unspecified plus intracranial haemorrhage	3
Pneumonia, post-asphyxial	4
Pneumonia, post-asphyxial plus intracranial haemorrhage	2
Bronchopneumonia	3
Bronchopneumonia plus intracranial haemorrhage	4
Bronchopneumonia plus thrush oesophagitis	1
Septic inhalation pneumonia ...	3
Septic inhalation pneumonia plus intracranial haemorrhage	3
Septic staphylococcal pneumonia ...	4
Septic staphylococcal pneumonia plus intracranial haemorrhage	2
Septic staphylococcal pneumonia following skin infection	3
	34
7. Meningitis, *B. coli*	2
8. Gastro-enteritis	9
Gastro-enteritis plus pneumonia ...	2
	11
9. Congenital syphilis	1
10. Other causes:	
Exsanguination	2
Massive pulmonary haemorrhage ...	1
Suprarenal haemorrhage	1
Meconium peritonitis	1
Gastric ulceration and haemorrhage	1
Accidental asphyxia	1
	7
Total	204

TABLE III.

Deaths by Birth-weights

(a) *Number of deaths*	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	5 pounds 9 ounces and over	All weights·
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2. Congenital defects	5	10	26	41
3. Prematurity	33	6	0	39
4. Asphyxia	13	22	10	45
(4a. Asphyxia plus subdural haemorrhage)	(7)	(9)	(4)	(20)
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7. Meningitis	0	0	2	2
8. Gastro-enteritis	2	5	4	11
9. Congenital syphilis	0	1	0	1
10. Other causes	2	4	1	7
Total	71	71	62	204
(b) *Percentages*				
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2. Congenital defects	7.0	14.1	41.9	20.1
3. Prematurity	46.5	8.4	0.0	19.1
4. Asphyxia	18.3	31.0	16.1	22.1
5. Intracranial haemorrhage ...	0.0	5.6	6.5	3.9
6. Pneumonia	21.1	16.9	11.3	16.7
8. Gastro-enteritis	2.8	7.0	6.5	5.4
10. Other causes (including meningitis and congenital syphilis)	2.8	7.0	4.8	4.9
Total	100.0	100.0	100.0	100.0
(c) *Rates per 1,000 births.*				
1. Erythroblastosis	10	14	0.12	2.1
2. Congenital defects	51	19	0.39	5.4
3. Prematurity	333	12	0.00	5.1
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These figures further emphasize the comparatively minor role that treatment after

TABLE IV.

Age at Death by Cause of Death.

Cause of death	Percentage of deaths by the end of:			
	1st day	2nd day	3rd day	1st week
Congenital defects and erythroblastosis	36.8	50.8	57.8	82.4
Prematurity	66.7	79.5	89.7	97.4
Asphyxia	64.4	88.8	93.2	95.5
Intracranial haemorrhage	25.0	75.0	75.0	100.0
Pneumonia	8.8	26.4	38.2	61.8
Gastro-enteritis	0.0	0.0	0.0	0.0

birth plays in the reduction of neonatal mortality beyond the level at present attained under good hospital conditions. As has been previously shown, deaths in the first 48 hours are little affected by improvements in treatment, and deaths from gross congenital defect are also obviously not amenable to any measures taken postnatally. It would therefore appear that the most effective further improvement in postnatal treatment of the infant would be measures to prevent the later infections.

4. *Cause of Death in Relation to Complications of Pregnancy.*

Table V and Fig. 2 show the incidence of toxaemia, antepartum haemorrhage and

of babies with congenital defects is only slightly greater than among mothers of infants who survived. With every other
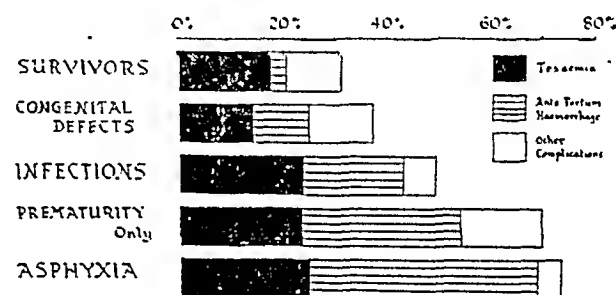
FIG. 2.

Cause of death in relation to maternal complications.

cause of death the incidence of complications is much higher. Of babies dying from prematurity over 50 per cent of the mothers

TABLE V.

Cause of Death by Complications of Pregnancy.

Cause of death	None per cent	Toxaemias, per cent	Antepartum haemorrhage, per cent	Others, per cent	Total, per cent
Congenital defects and erythroblastosis	63.1	14.0	10.5	12.3	100.0
Prematurity	30.8	23.1	30.8	15.4	100.0
Asphyxia	26.7	24.4	44.4	4.4	100.0
Intracranial haemorrhage	25.0	62.5	0.0	12.5	100.0
Infections	51.0	23.4	19.2	6.4	100.0
Other causes	37.5	12.5	25.0	25.0	100.0
Survivors	69.2	17.1	3.0	10.7	100.0

other complications in the mother, for infants who died from certain specified conditions, in comparison with their incidence in mothers of babies who survived. The incidence of complications among mothers

suffered from toxaemia or antepartum haemorrhage, and in the case of asphyxia the proportion was more than 70 per cent, antepartum haemorrhage being associated with 44 per cent of these deaths. By con-

trast, the incidence of these complications in the mothers of survivors was 17 per cent of toxaemia, and 3 per cent of antepartum haemorrhage. The high toxaemia rate seen in cases of intracranial haemorrhage is associated with a greater frequency of forceps delivery in women with toxaemia. The percentage is based on only 6 cases.

5. *Cause of Death in Relation to mode of Delivery.*

Table VI compares the incidence of different modes of delivery in cases of death

aetiological factor was adjudged to be asphyxia or birth trauma. Gross subdural haemorrhage due to birth injury is seen to occur with much the most frequency in mature deaths, though the contrast is not so marked with slight degrees of haemorrhage. On the other hand, subarachnoid, intraventricular and intracerebral haemorrhages, either alone or in combination, occur almost exclusively in premature infants. These latter forms of haemorrhage are most probably due to asphyxia, and occur more commonly in premature infants

TABLE VI.

Cause of Death by Mode of Delivery.

Cause of death	Spontaneous vertex, per cent	Instrumental, per cent	Breech, per cent	Caesarean section, per cent	Total, per cent
Congenital defects and erythroblastosis	66.7	5.3	19.2	8.8	100.0
Prematurity	59.0	0.0	23.1	17.9	100.0
Asphyxia	53.3	2.2	28.9	15.6	100.0
Intracranial haemorrhage	12.5	50.0	37.5	0.0	100.0
Infections	68.1	14.9	14.9	2.1	100.0
Other causes	62.5	0.0	12.5	25.0	100.0
Survivors	66.7	13.4	4.6	3.8	100.0

from certain specified causes with that obtained in infants who survived. The main points to be noted are :

The high incidence of breech delivery in infants dying of congenital defects, prematurity, asphyxia and intracranial haemorrhage. In the first 2 conditions the mode of delivery is most likely a consequence of the abnormal foetus, whereas deaths due to asphyxia and intracranial haemorrhage were probably directly due to the breech delivery.

Intracranial Haemorrhage.

Table VII shows the total number of cases in which intracranial haemorrhage was found, irrespective of whether or not the haemorrhage was considered to be the cause of death, or whether the principal

because of incomplete development of muscle and elastic tissue in the walls of the veins.

Section (c) of the table shows the incidence of different forms of haemorrhage per 1,000 live births according to mode of delivery. A high proportion of all types of intracranial haemorrhage was found in breech deliveries. This may be accounted for by the relatively large number of premature infants delivered by the breech, and to the special dangers in this mode of delivery of asphyxia, and of too rapid delivery of the head.

Pneumonia.

The diagnosis "pneumonia" in this classification covers a number of conditions:

TABLE VII.

Deaths from Intracranial Haemorrhage.

	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	Over 5 pounds 8 ounces	Total
(a) *Numbers of cases.*				
Subdural	1	4	8	13
Subdural (slight)	5	7	5	17
Subarachnoid	5	2	1	8
Intraventricular	10	4	0	14
Multiple (subarachnoid and/or intraventricular and/or intracerebral)	9	3	0	12
Intradural	0	0	1	1
Total	30	18	17	65
(b) *Deaths as percentage of total weight in group.*				
Subdural	1.4	5.6	12.9	
Subdural (slight)	7.0	7.0	11.3	
Subarachnoid	7.0 ⎫	2.8 ⎫	1.6 ⎫	
Intraventricular	14.1 ⎬ 33.8	5.6 ⎬ 12.6	0.0 ⎬ 1.6	
Multiple	12.7 ⎭	4.2 ⎭	0.0 ⎭	
Intradural	0.0	0.0	1.6	

	Spontaneous vertex	Instrumental	Breech	Caesarean
(c) *Deaths per 1,000 live births by mode of delivery.*				
Subdural	0.5	7.6	13.9	0.0
Subdural (slight)	1.5	3.2	17.4	3.8
Multiple	4.4	0.0	31.4	3.8
Total	6.4	10.8	62.7	7.6

1. Postasphyxial, occurring in a lung which is already atelectatic or filled with liquor amnii.

2. Bronchopneumonia, occurring either in the form commonly seen in elderly infants, or in a massive confluent form.

3. Septic staphylococcal pneumonia, with multiple suppurating foci, sometimes resulting from septic skin infections and septicaemia.

4. Septic inhalation pneumonia resulting from aspiration of milk or regurgitation of stomach contents.

5. Pneumonia not further specified.

6. Inhalation of excessive liquor amnii and vernix in an asphyxiated infant with commencing inflammatory changes. These cases died before gross pneumonic changes could occur.

Types 1 to 5 are listed under " pneumonia " in the previous classification, and type 6 under " asphyxia ".

The numbers of the different types of pneumonia found in the 204 deaths were as follows :

Postasphyxial pneumonia	7
Bronchopneumonia	8
Septic staphylococcal pneumonia	8
Septic inhalation pneumonia	6
Unspecified pneumonia	6
Inhalation and inflammation	16
Total	51

Over 90 per cent of cases of inhalation with inflammatory changes and of post-

asphyxial pneumonia died within 48 hours of birth, whereas 86 per cent of the cases of septic staphylococcal, septic inhalation and bronchopneumonia died after the third day, and 55 per cent of them after the end of the first week.

STILLBIRTHS.

The number of stillbirths recorded was 373. A case was considered to be a stillbirth if the estimated length of gestation was 28 weeks or longer, irrespective of weight at birth. Table IX gives the

TABLE VIII.

Deaths and Stillbirths from Congenital Defects by Maternal Age.

	Primiparae		Multiparae	
Age of mother	Number of cases	Rate per 1,000 births	Number of cases	Rate per 1,000 births
15 to 19	6	16.6	—	—
20 to 24	25	10.4	5	15.6
25 to 29	14	10.0	11	15.7
30 to 34	7	13.0	17	21.8
35 to 39	7	27.3	14	24.8
40 to 44	—	—	5	22.3

Congenital Defects and Age of Mother. Deaths and Stillbirths.

Table VIII shows the number of fatal congenital defects and the rate per 1,000 births according to maternal age. There appears to be a rise in the death-rate for mothers over 30 in both primiparae and multiparae. The rates for mothers under 30 and over, are as follows:

Primiparae :
    Under 30.   10.8 per 1,000 births
    30 and over   17.0 per 1,000 births

Multiparae :
    Under 30   15.8 per 1,000 births
    30 and over   22.9 per 1,000 births

On applying a combined probability test the 2 differences, considered together, are found to be just significant, in spite of the small number of cases. The rise with age of mother is in accord with the findings of Penrose (1946) that increasing maternal age is significantly related to the incidence of anencephaly, spina bifida and congenital hydrocephalus, and of Malpas (1937) who made a similar observation for congenital deformities as a whole.

causes of stillbirth in detail. In selecting asphyxia and intracranial haemorrhage as the primary cause of the stillbirth, the same criteria were used as in the classification of

TABLE IX.   *Causes of Stillbirths.*

1. Erythroblastosis foetalis		6
2. Congenital defect		71
3. Asphyxia	53	
Asphyxia plus subdural haemorrhage	22	
Asphyxia plus subarachnoid and/or intraventricular haemorrhage ...	2	
Asphyxia plus intraperitoneal haemorrhage	1	
Asphyxia plus pneumonic changes ...	3	
	—	81
4. Subdural haemorrhage	7	
Subdural plus intraperitoneal haemorrhage	1	
Subdural plus subarachnoid haemorrhage	1	
Subdural haemorrhage plus slight asphyxia	2	
	—	11
5. Congenital syphilis	2	2
6. Other causes:		
Prematurity only	3	
Fractured spine	1	
Exsanguination	1	
	—	5
7. Intrauterine death with maceration		75
8. No autopsy: cause unknown		122
Total		—
		373

deaths. Diagnosis was made on autopsy findings in 103 cases. Further diagnoses were made as follows:

Obvious congenital defect	61
Asphyxia diagnosed clinically	8
Intracranial haemorrhage diagnosed clinically following difficult delivery	3
Fractured spine diagnosed clinically	1

A definite diagnosis was thus obtainable in 176 cases. In a further 75 cases death occurred in utero before commencement of labour, a macerated foetus being produced. In 122 cases the pathological cause of death was not ascertained. Table X gives causes of stillbirth in relation to weight of foetus.

parison with the incidence of complications in the mothers of babies who survived. The points to be noted are:

1. The high incidence of hydramnios occurring with congenital defects, the defect nearly always being anencephalus.

2. In cases of intrauterine death the toxaemia rate is twice as high as in the survivor group, and higher than that associated with any other cause of stillbirth or infant death. This suggests that maternal toxaemia may be an important aetiological factor in these cases.

3. In those stillbirths for which no pathological diagnosis of cause of death was

TABLE X.

Causes of Stillbirth by Birth-weight.

(a) *Numbers of cases.*	Below 3 pounds 9 ounces	3 pounds 9 ounces to 5 pounds 8 ounces	5 pounds 9 ounces to 8 pounds 15 ounces	Over 8 pounds 15 ounces	Total
Erythroblastosis foetalis	2	2	2	0	6
Congenital defects	34	16	19	2	71
Asphyxia	6	16	48	11	81
Subdural haemorrhage	0	2	6	3	11
Congenital syphilis	0	1	1	0	2
Other causes	3	1	1	0	5
Intrauterine death	25	17	28	5	75
No autopsy; cause unknown	21	31	64	6	122
Total	91	86	169	27	373
(b) *Percentages*					
Erythroblastosis foetalis	2.2	2.3	1.2	0.0	1.6
Congenital defects	37.4	18.6	11.2	7.4	19.0
Asphyxia	6.6	18.6	28.4	40.7	21.7
Subdural haemorrhage	0.0	2.3	3.6	11.1	2.9
Congenital syphilis and other causes ...	3.3	2.3	1.2	0.0	1.9
Intrauterine death	27.5	19.8	16.6	18.5	20.1
No autopsy: cause unknown	23.1	36.1	37.9	22.2	32.7
Total	100.0	100.0	100.0	100.0	100.0

1. *Causes of Stillbirth in Relation to Complications of Pregnancy.*

Table XI shows the presence or absence of complications of pregnancy in the mother in stillbirth due to various causes, in com-

made, the toxaemia rate was twice that of the survivor group, and the rate for antepartum haemorrhage was 6 times as high. Had autopsies been performed it is likely that where the mother had antepartum

TABLE XI.

Causes of Stillbirth by Complications of Pregnancy.

Cause of stillbirth	No complications per cent	Toxaemia per cent	Ante-partum haemorrhage per cent	Hydramnios per cent	Others per cent	Total per cent
Congenital defects and erythroblastosis ...	40.3	9.1	9.1	32.5	9.1	100.0
Asphyxia	48.2	25.9	22.2	—	3.7	100.0
Subdural haemorrhage	81.8	18.2	—	—	—	100.0
Intrauterine death	56.0	34.7	4.0	—	5.3	100.0
Cause unknown ...	38.8	33.1	23.1	1.7	3.3	100.0
Survivors	69.2	17.1	3.0	1.1	9.6	100.0

haemorrhage the cause of death would have usually been found to be asphyxia.

4. The figures for subdural haemorrhage are based on only 11 cases, and no great importance can be attached to the apparently greater freedom from complications of pregnancy.

2. *Causes of Stillbirth in Relation to Mode of Delivery.*

Table XII shows the mode of delivery in stillbirths from specified causes, in comparison with a control group of babies who survived.

The category " subdural haemorrhage " in this Table covers all cases not specifi-

cally classified as " slight," including those in which the principal cause of the stillbirth was adjudged to be asphyxia. The main points to be noted are as follows:

1. The high incidence of breech delivery in all categories of stillbirth. The congenital defects occurring with breech delivery were mainly cases of hydrocephalus, microcephalus and anencephalus. Here the mode of delivery is most likely a consequence of the congenital defect. A similar consideration applies to cases of intrauterine death. In stillbirths due to asphyxia and subdural haemorrhage the high incidence of breech delivery is aetiologically important.

2. The high incidence of instrumental

TABLE XII.

Causes of Stillbirth by Mode of Delivery.

Cause of stillbirth	Spontaneous vertex per cent	Instrumental per cent	Breech per cent	Caesarean section per cent	Craniotomy per cent	Total per cent
Congenital defects and erythroblastosis ...	68.8	1.3	14.3	1.3	14.3	100.0
Asphyxia	50.8	17.4	20.6	7.9	3.2	100.0
Subdural haemorrhage (total)	20.7	44.8	27.6	6.9	0.0	100.0
Intrauterine death ...	63.9	5.3	14.7	1.3	14.7	100.0
Cause unknown ...	52.9	19.8	14.0	5.0	8.3	100.0
Survivors	78.2	13.4	4.6	3.8	0.0	100.0

delivery, amounting to 45 per cent of all cases, in stillbirths with subdural haemorrhage. Instrumental or breech delivery occurred in nearly three-quarters of the stillbirths from this cause.

Deaths and Stillbirths in Relation to Sex of Infant.

It was shown in the first paper in this series that although there is a higher prematurity-rate among females, male infants have a lower survival-rate, especially in the smaller weight groups. Table XIII gives

but for every other cause of death the males had a higher rate. This is most marked in prematurity, asphyxia and neonatal infections. The sex-disparity becomes even more striking when account is taken of the effect of birth-weight. These causes of death tend to be more frequent in the smaller babies, but although the boy babies as a group are heavier than the girls, they show a considerably higher mortality.

The total stillbirth-rate is approximately the same for males and females. The female rate for congenital defects of 11.4 is 4.8 per 1,000 higher than the male rate,

TABLE XIII.
Deaths and Stillbirths by Sex of Infant.

			Number of cases			Rate per 1,000 births	
	Male	Female	Unstated	Total	Male	Female
(a) *Deaths*						
Congenital defects	21	19	1	41	5.4	5.6
Erythroblastosis	11	5	—	16	2.8	1.5
Prematurity	28	9	2	39	7.2	2.6
Asphyxia	31	14	—	45	8.0	4.1
Subdural haemorrhage ...	5	3	—	8	1.3	0.9
Infections	32	13	2	47	8.3	3.8
Other causes	5	3	—	8	1.3	0.9
Total deaths	133	66	5	204	34.3	19.4
(b) *Stillbirths.*						
Congenital defects	27	40	4	71	7.0	11.8
Erythroblastosis	3	2	1	6	0.8	0.6
Asphyxia	48	31	2	81	12.4	9.1
Subdural haemorrhage ...	8	3	—	11	2.1	0.9
Intrauterine death	40	33	2	75	10.3	9.7
Intrauterine death	3	4	—	7	0.8	1.2
Cause unknown	67	54	1	122	17.3	15.9
Total stillbirths	196	167	10	373	50.7	49.2

the numbers of deaths and stillbirths and the rates per 1,000 total births by cause for male and female infants.

The death-rate per 1,000 for female infants was 19.4 compared with 34.3 for males, giving a male excess of 14.9 per 1,000 births. The rate for congenital defects is approximately the same in the 2 sexes,

mainly because of the excess of cases of anencephaly among the females. For every other cause of stillbirth the males have a higher rate, though the disparity is not so great as in the case of deaths after delivery.

It would appear that female infants are the better able to withstand the hazards of

Death-Rate per 1000 Total Births

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |

PREMATURITY Only

INFECTIONS

ASPHYXIA

CONGENITAL DEFECTS

OTHERS
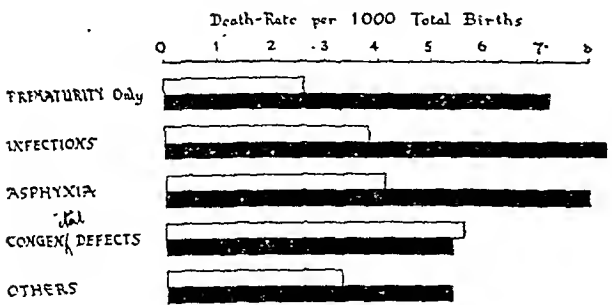
FIG. 3.
Death-rates according to sex.
Outlined rectangles—Females.
Black rectangles—Males.

diagnosis. In this section an attempt is made to assess the primary cause of wastage. Each death and stillbirth has been considered separately, and all the factors influencing the outcome have been taken into account before a decision has been made on what comprised the primary and most important cause of the fatality. The findings for deaths are shown in Table XIV, and for stillbirths in Table XV, while Fig. 4 shows the main conclusions in graphical form.

It has already been shown in Part I how chances of survival depend largely on the weight of the infant at birth, and how the various complications of pregnancy predispose to premature labour. Where one

the birth process and adaptation to a new environment than are male infants.

Death-rates for male and female infants from the main cause groups are shown in Fig. 3.

TABLE XIV.

Primary Causes of Death.

1. Congenital defects	41
2. Erythroblastosis foetalis	16
3. Prematurity (below 4½ pounds)	101
due to antepartum haemorrhage 15	
,, ,, ,, , death from asphyxia 16	
,, ,, ,, , death from infection 6	
due to toxaemia 18	
,, ,, , death from infection 6	
due to hydramnios 4	
due to early Caesarean section for acute abdomen 1	
Cause unknown, death from infection 10	
Cause unknown 25	
4. Asphyxia (over 4½ pounds)	15
due to antepartum haemorrhage 5	
,, ,, ,, , death from infection 2	
due to prolonged labour 3	
due to Caesarean section 1	
Cause unknown, associated with toxaemia 3	
accidental asphyxia 1	
5. Subdural haemorrhage due to birth trauma	12
Breech delivery 5	
Forceps delivery 5	
Manual rotation and forceps delivery 2	
6. Neonatal infection (over 4½ pounds)	18
7. Congenital syphilis	1
Total	204

Primary Cause of Wastage.

In previous sections the causes of death and stillbirth have been given by pathological findings at autopsy or on clinical

of these complications has resulted in the birth of a premature infant which did not survive, the primary cause is considered to the complication, irrespective of what

TABLE XV.

Primary Causes of Stillbirths.

1. Congenital defects		71
2. Erythroblastosis foetalis		6
3. Prematurity (below 4½ pounds)		85
due to toxaemia	39	
due to antepartum haemorrhage	22	
Cause unknown	24	
4. Postmaturity		3
5. Asphyxia (over 4½ pounds)		63
due to toxaemia	11	
due to antepartum haemorrhage	27	
associated with breech delivery	2	
,, ,, version and extraction	4	
,, ,, forceps delivery	1	
,, ,, Caesarean section	1	
,, ,, prolonged labour	10	
,, ,, ruptured uterus	1	
,, ,, true knot in cord	1	
Cause unknown	5	
6. Subdural haemorrhage		26
spontaneous vertex delivery with complications	4	
breech delivery	7	
version and extraction	8	
forceps, including failed forceps outside	7	
7. Hydramnios		2
8. Diabetes—intrauterine death		2
9. Congenital syphilis		2
10. No autopsy—associated with complications of delivery ...		53
complications necessitating craniotomy	22	
premature separation of placenta	1	
prolapsed cord	12	
prolonged labour	9	
contraction ring	2	
deep transverse arrest	5	
tonic uterine contractions	1	
fractured spine due to difficult delivery	1	
11. No autopsy—Cause unknown		60
associated with Caesarean section	1	
,, ,, forceps delivery	4	
,, ,, breech delivery	4	
,, ,, version and extraction	6	
,, ,, toxaemia and Caesarean section	2	
,, ,, ,, ,, forceps delivery	2	
,, ,, ,, ,, breech delivery	5	
,, ,, ,, ,, spontaneous vertex delivery	14	
spontaneous vertex delivery	22	
Total		373

was the pathological cause of death. Although the upper limit of prematurity is generally taken to be 5½ pounds, the larger premature infants stand a good chance of surviving. It was therefore decided to assume that for infants of 4½ pounds or less the presence of the prematurity itself was likely to be the most important factor in causing death or stillbirth, but between 4½ and 5½ pounds some other factor such as infection or birth trauma would be the more decisive in cases that did not survive. For
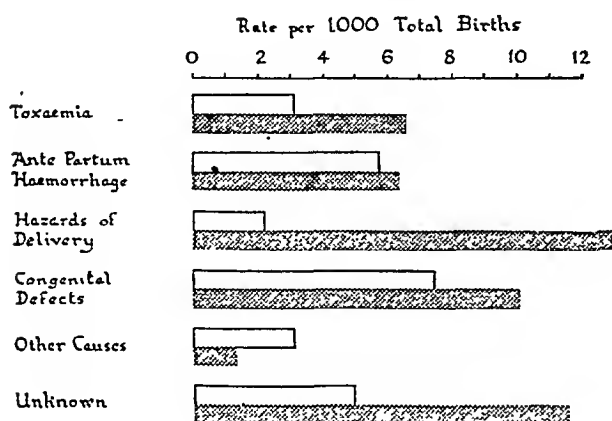
FIG. 4.
Primary causes of wastage.
Outlined rectangles—Deaths.
Black rectangles—Stillbirths.

known ''. On the other hand, among the 18 cases under the heading '' neonatal infection '', there were a number of cases between $4\frac{1}{2}$ and $5\frac{1}{2}$ pounds, the primary cause in these instances being regarded as infection rather than prematurity.

In the deaths a definite decision could be made in every case. Among the stillbirths, owing to the much smaller proportion of autopsies, this was not always possible. In 53 of the cases for which autopsy was not performed, there was some complication of delivery of sufficient severity to be a likely cause of stillbirth. In the remaining 60 cases without autopsy, the diagnosis of cause of stillbirth is doubtful. Fifteen were delivered by the breech, forceps or Caesarean section, and it is possible that the mode of delivery was responsible for the stillbirth. Nine more

example, Table XIV lists 10 cases of deaths from infection in infants below $4\frac{1}{2}$ pounds, in whom the cause of prematurity was unknown. These cases are considered to be

TABLE XVI.

Primary Causes of Wastage.

Cause of wastage	Numbers of cases.			Percentages			Per 1,000 births		
	Deaths	Still-births	Total	Deaths	Still-births	Total	Deaths	Still-births	Total
Congenital defects	41	71	112	20.1	19.0	19.4	5.4	9.3	14.7
Erythroblastosis	16	6	22	7.8	1.6	3.8	2.1	0.8	2.9
Toxaemias	24	50	74	11.8	13.4	12.8	3.1	6.6	9.7
Antepartum haemorrhage	44	48	93	21.6	13.1	16.1	5.8	6.4	12.2
Hydramnios	4	2	6	2.0	0.5	1.0	0.5	0.3	0.8
Neonatal infection	18	—	18	8.8	—	3.1	2.4	—	2.4
Congenital syphilis ...	1	2	3	0.5	0.5	0.5	0.1	0.3	0.4
Diabetes	0	2	2	0.0	0.5	0.3	0.0	0.3	0.3
Postmaturity	0	3	3	0.0	0.8	0.5	0.0	0.4	0.4
Hazards of delivery ...	17	99	116	8.3	26.5	20.1	2.3	13.0	15.3
Accidental asphyxia ...	1	0	1	0.5	0.0	0.2	0.1	0.0	0.1
Possible cause:									
Toxaemias	3	14	17	1.5	3.8	2.9	0.4	1.8	2.2
Toxaemia plus hazards of delivery	0	9	9	0.0	2.4	1.6	0.0	1.2	1.2
Hazards of delivery ...	0	15	15	0.0	4.0	2.6	0.0	2.0	2.0
Cause unknown	35	51	86	17.2	13.8	14.9	4.6	6.7	11.3
Total	204	373	577	100.0	100.0	100.0	26.8	49.1	75.9

primarily deaths from prematurity, and not from infection, and as the cause of prematurity is not known, they are classified in Table XVI under '' cause unknown ''. On the other hand, among the came of mothers with toxaemia of pregnancy, as well as having an abnormal delivery. A further 14 cases from toxaemic mothers had a spontaneous vertex delivery,

D

with no complicating factors. There were 22 cases with a normal delivery, and no accompanying abnormalities either during pregnancy or labour; for these the cause of stillbirth is quite unknown.

Table XVI shows the primary causes of death and stillbirth, as given in Tables XIV and XV, classified into 11 groups with a further 3 groups where a possible cause is suggested. It is seen that congenital defects plus erythroblastosis are responsible for nearly 24 per cent of all deaths and stillbirths, toxaemia and antepartum haemorrhage in the mother for 30 per cent, hazards of delivery for 20 per cent, while all other causes account for only 6 per cent. In 22 per cent of the cases the cause of wastage was unknown.

PROSPECTS OF REDUCTION OF THE STILLBIRTHS AND NEONATAL DEATH-RATE.

In considering the results of the investigation on the prospect of further reducing stillbirth and infant death-rates, the problem can be approached from the following four angles:

1. *Postnatal Measures.*

Postnatal care of the infant may be directed to special treatment of premature babies, prevention of infection, and the treatment of trythroblastosis foetalis. The premature babies in this series of cases were nursed under excellent conditions in air-conditioned incubator-rooms, under the supervision of paediatricians and nurses experienced in the care of very small babies. Comment has already been made on the fact that no further improvement in treatment appears to be of much avail in saving premature infants who die within 48 hours of birth, and it seems unlikely that the death-rate of the minority who sur-

vived to die later could be much further reduced.

Only 18 deaths were directly attributable to infection. These deaths, which occurred in infants over 4½ pounds who had no other complicating factor might possibly have been prevented, but that would only have reduced the death-rate by 2.4 per 1,000 births. Recent research has discovered a cause and treatment for erythroblastosis foetalis, and cases which in the past would have died, may now be saved. But here again the cases form only a small proportion of the total wastage-rate. In short, at the best the reduction of the neonatal death-rate that is possible by postnatal measures can deal only with a fraction of the problem.

2. *Measures During Labour and Delivery.*

Death amounting to 2.2 and stillbirths to 13 per 1,000 births were attributed to hazards of delivery, this being about one-fifth of the total wastage. Many of these cases were admitted as emergencies, and might have been saved given more adequate antenatal supervision with early diagnosis and correction of abnormalities.

3. *Measures During or Before Pregnancy.*

Abnormal conditions in the mother, toxaemia of pregnancy and antepartum haemorrhage, accounted for nearly one-third of the total wastage. A reduction in the incidence of these 2 conditions would lead to a substantial lowering in the infant death- and stillbirth-rates. Maternal death-rates from these complications have fallen since 1939, and this may be taken as an indication of lowered case-incidents. Though this fall may be due in part to better antenatal care, it is probable that it is largely the result of better nutrition of mothers during the war. It is hoped in a further paper to deal with the effect of

social and economic factors on prematurity. There is already a considerable body of evidence on the important effect of such factors as housing, nutrition, employment of pregnant women and poverty on infant death- and stillbirth-rates, as for example in the papers by Woolf and Waterhouse (1945) and Baird (1945).

4. *Conditions at Present not Amenable to Treatment.*

Nearly one-fifth of the total wastage was due to congenital defects. In the present state of our knowledge these deaths are not preventable, though a new line of research was opened up by Gregg (1941), when he described an association between maternal infection during the early months of pregnancy and defect in the infant. This is a field which should amply repay further investigations.

SUMMARY.

This paper comprises Part III in a series of studies based on nearly 8,000 births in the Simpson Memorial Pavilion, Edinburgh, during the years 1943 to 1945 inclusive, and deals with deaths and stillbirths.

Recorded deaths were 204, 142 in premature and 62 in mature infants. Of the 373 stillbirths, 177 were premature and 195 were mature or postmature. Nearly one-quarter of the premature deaths took place in the first 6 hours and one half on the first day; 25 per cent of mature deaths occurred during the first day.

Among premature infants the commonest causes of death were prematurity alone, asphyxia and pneumonia, while congenital defects accounted for the majority of the mature deaths. Congenital defects and asphyxia were the commonest pathological findings in stillbirths for both premature and mature infants, but in over half the cases there was no pathological diagnosis. There was a much higher incidence of complications of pregnancy in the mothers of babies who died as compared with those who survived. The same is true for abnormal forms of delivery. A detailed analysis of these cases is given according to the nature of complication or method of delivery and pathological cause of death or stillbirth.

Death-rates for congenital defects are about the same for males and females but for every other cause boys show a higher rate. Females have a higher stillbirth-rate from congenital defects, mainly due to excess anencephalus, but males have a higher rate from every other cause. Total rates per 1,000 births were:

Deaths: males 34.3; females 19.4.
Stillbirths: males 50.6; females 49.1.

Intracranial haemorrhage was found at autopsy in 65 out of the 204 infant deaths. Subdural haemorrhage was commonest in larger babies and, unless mild, associated with birth trauma. Subarachnoid, intraventricular and intracerebral haemorrhage occurred almost exclusively in prematures, and was associated with asphyxia.

There was a rise in the death- and stillbirth-rate from congenital defects with increasing maternal age.

An attempt has been made to assess what was the primary cause of each case of death or stillbirth. Of total cases of wastage: 24 per cent were attributed to congenital defects; 13 per cent to toxaemias of pregnancy; 16 per cent to antepartum haemorrhage; 20 per cent to hazards of delivery; 6 per cent to all other causes.

Finally, suggestions have been made, based on the above results, of possible ways of reducing stillbirth- and neonatal death-rates.

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A Further Contribution to the Study of the Influence of Failure of Müllerian Duct Fusion on Pregnancy and Labour

BY

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IN 1945 I published a paper on this subject describing the effects of minor uterine deformities on pregnancy and labour in 18 patients. In that paper I drew attention to several important facts. Firstly, these deformities are more common than textbooks would lead one to think. Secondly, they expose the mother and foetus to certain hazards, many of which can be guarded against if the deformity is recognized. Thirdly, the chief of these abnormalities is transverse lie, repeated abortions and an increased risk of retention of the placenta. At the time of writing that paper I described 3 women who were then undelivered. Since that time I have seen 19 further cases, and the object of this paper is to give their clinical histories and review the 78 pregnancies which these 37 patients had between them.

Cases 16, 17 and 18 were described in my previous paper but were delivered after its publication. It is sufficient here to describe the ultimate outcome of these 3 cases.

CASE 16. This patient had a normal delivery and was found to have a uterus bicornis unicorpus unicollis.

CASE 17. This patient had a normal delivery and also had a uterus bicornis unicorpus unicollis.

CASE 18. Premature labour at 34 weeks. Child an anencephalic monster. Here again the patient had a uterus bicornis unicorpus unicollis.

In the year that followed the publication of my first paper I met with 19 further examples of this deformity. There was no special selection of cases in this series and 15 of them were discovered among 1,200 routine cases in the antenatal clinic. This is an incidence of 1 in 78 cases. This apparent increased incidence was undoubtedly due to the fact that we were looking for them and I think there can be few that escaped our notice. Sometime ago, when visiting another maternity hospital, the resident obstetrician showed me some antenatal cases and one of these presented the typical uterine deformity. These findings lend support to my previous statement that they are relatively common.

CASE 19. Age 31; 2 gravida.

Pregnancy 1. Normal delivery of a 9 pounds infant.

Pregnancy 2. At 36 weeks uterine deformity was noticed and the baby was presenting as a breech. In the circumstances version was not attempted. The membranes ruptured 4 days before the onset of pains. A normal breech delivery took place after 12 hours of labour. The placenta was retained and there was a severe postpartum haemorrhage. Crede's expression of the placenta was done. Good recovery. Male child weighing 7 pounds 7½ ounces.

CASE 20. Age 29; 1-gravida.

Pregnancy 1. Repeated transverse lie throughout the antenatal period. Version was performed many times but the transverse lie always recurred. The day before labour commenced spontaneous cephalic version took place and the patient had

a normal delivery. The placenta was retained for 2½ hours but there was no haemorrhage. Living female child weighing 8 pounds 7 ounces.

CASE 21.   Age 41; 2-gravida.

Pregnancy 1.   Normal delivery of a 9½ pounds baby 12 years prior to the second pregnancy.

Pregnancy 2.   Uterine deformity diagnosed 6 weeks before term. Repeated transverse lie throughout the last 4 weeks of pregnancy. Spontaneous version the day before labour commenced. Vertex presentation and normal delivery of a living male child weighing 7 pounds 8 ounces. Placenta retained for 1 hour 10 minutes, but there was no haemorrhage.

Whilst congratulating myself on the results of my conservatism in this case (I had been urged by a colleague to perform Caesarean section) I had no forewarning of the sequel which was nearly to cost the patient her life. Despite the fact that the puerperium was normal and that the lochia stopped on the 10th day, a small portion of a cotyledon of placenta was retained and was overlooked at the routine examination following the third stage. Three weeks after discharge she was re-admitted with a small secondary postpartum haemorrhage. I curetted this patient and found organizing placental remnants in the right cornu firmly adherent to the uterine wall. As soon as I dislodged some of the fragments a torrential haemorrhage began. I was unable to reach the cornu with a finger or to remove all the fragments with the curette. In 10 minutes, despite packing the uterus, this patient lost 6 pints of blood, excluding clots. The collapse associated with this tremendous bleeding was very severe and the patient was soon *in extremis*. Transfusion was started in all 4 limbs at once, and under pressure 8½ pints of blood were transfused in 14 minutes. In view of the patient's age I had no hesitation in performing subtotal hysterectomy and by this means the bleeding was controlled. Altogether she received 15 pints of blood in 4 hours (10 of them in the first 25 minutes) and by the end of the operation her pulse-rate was 130 and her blood-pressure 70/40. To digress for a moment, I would like to stress the importance of rapid transfusion in cases of rapid loss of blood such are encountered in midwifery. The object is to restore the blood volume to normal as rapidly as possible and where

active bleeding is taking place there is no danger of overloading the circulation by rapid transfusion. If a patient can lose 6 pints of blood in 10 minutes (and this quantity was measured and not guessed) to replace this by transfusing 1 pint in half-an-hour is obviously futile.

This patient made an excellent recovery from her operation and has remained well since. The specimen showed a uterus bicornis unicorpus unicollis with small placental fragments densely adherent to the right cornu and the placental site showed a large number of patent veins in its base.

CASE 22.   Age 22; 2 gravida.

Lobectomy for bronchiectasis at the age of 10. Bronchiestasis of opposite lung.

Pregnancy 1.   Normal delivery of 7½ pounds child.

Pregnancy 2.   Admitted in labour at 32 weeks with transverse lie and prolapsed hand. Obvious uterine deformity. Patient's general condition poor. Internal version and delivery of a stillborn female child weighing 4 pounds 10 ounces. Placenta retained for 1 hour. Postpartum haemorrhage then commenced which was checked at once by Crede's expression of the placenta. During the course of the version the placenta was found situated in the right cornu.

An autopsy was performed on the baby and its uterus was found to be, like its mother's, a uterus bicornis unicorpus unicollis very similar to the one I illustrated in my first paper.

CASE 23. Age 21; primigravida.

Patient attended the antenatal clinic where the deformity was diagnosed at the 20th week. The presentation was vertex throughout pregnancy and the head engaged at the 36th week. Normal delivery of a living female child weighing 6 pounds 4 ounces. The placenta was retained for 2 hours with severe postpartum haemorrhage. Manual removal of placenta which was situated in the right horn was done. There was delay in removing this placenta and the haemorrhage necessitated a blood transfusion.

CASE 24.   Aged 34; 3-gravida.

Pregnancy 1.   Abortion at 3 months.

Pregnancy 2.   Abortion at 3 months.

Pregnancy 3.   Uterine deformity noticed at 33rd week; presentation vertex. Normal labour and

normal delivery of a female child weighing 6 pounds 14 ounces. Third stage normal.

CASE 25. Aged 23; primigravida.

Uterine deformity noticed at 16 weeks. Presentation vertex throughout pregnancy. Patient had mitral stenosis and aortic regurgitation. Normal delivery of a female infant weighing 5 pounds 8 ounces. Third stage normal.

CASE 26. Aged 33; 6-gravida.
Pregnancy 1. Normal vertex; 7 pounds.
Pregnancy 2. Breech; 6½ pounds.
Pregnancy 3. Breech; 10 pounds.
Pregnancy 4. Vertex; 5½ pounds.
Pregnancy 5. Vertex 10 pounds.
Pregnancy 6. Admitted to hospital as an emergency in labour suffering from antepartum haemorrhage. On examination the uterus showed a well-marked fundal deformity, the child presented by the shoulder; there was a marginal placenta praevia present covering half of the os, which was three-quarters dilated. The fundus of the uterus was in tonic contraction. I decapitated the infant (a female weighing 6 pounds 14 ounces), delivered her and removed the placenta manually. This was an example of uterus bicornis unicorpus unicollis. The infant's uterus was normal. The right horn in this case was longer than the left.

CASE 27. Age 25; 2-gravida.
Pregnancy 1. Normal delivery: child's weight 7½ pounds.
Pregnancy 2. At 37 weeks the uterine deformity was noted and the baby presented as a breech. Version was unsuccessful. At term the patient was admitted in labour with an oblique breech presentation. After 8 hours in labour the membranes ruptured at full dilatation and the cord prolapsed. Immediate breech extraction of a living female infant weighing 6 pounds 9 ounces. The head of this foetus· was in the left horn of the uterus as was also the upper margin of the placenta. The remainder of the placenta lay on the posterior wall and the lower border almost reached the lower segment. The third stage was normal and lasted only 10 minutes.

CASE 28. Aged 28; 2-gravida.
Pregnancy 1. Premature labour at 30 weeks.
I operated on this patient for a ruptured ectopic gestation and performed a left salpingectomy.

There was a depression at the fundus which was well marked even though the uterus was not greatly enlarged.

CASE 29. Age 23; 2-gravida.
Pregnancy 1. Abortion at 3 months.
Pregnancy 2. First seen at 39 weeks. Obvious uterine deformity and a transverse lie. Version attempted without anaesthesia but failed. At term version under anaesthesia failed to correct the transverse lie. Labour commenced and the transverse lie still could not be corrected. Lower segment Caesarean section was done and a living female child weighing 6 pounds was born. The placenta was on the posterior and left lateral walls but did not reach to the lower segment.

CASE 30. Age 30; 2-gravida.
·*Pregnancy 1.* Normal delivery of 6 pounds baby after trial labour for persistent non-engagement of the head.
Communication with the hospital where this delivery took place showed that the deformity had not been recognized.
Pregnancy 2. At 34 weeks the deformity was very obvious and the baby lay as an oblique breech. Version failed. At 36 weeks the presentation was transverse. At 38 weeks it was again an oblique breech. Version under anaesthesia failed. Lower segment Caesarean section was done at term. A living male child weighing 8 pounds was born. The placenta lay on the right lateral wall and reached almost to the lower segment. This patient was a sister of Case 7 described in the previous series.

CASE 31. Age 30; 2-gravida.
·*Pregnancy 1.* Abortion at 8 weeks.
Pregnancy 2. Threatened abortion at 8 weeks and again at 12 weeks. The abnormal uterine contour became obvious at 24 weeks. Toxaemia at term. Vertex presentation. Induction of labour. Stillborn male child. Placenta retained with slight haemorrhage and severe obstetric shock; treated by blood transfusion. Manual removal of placenta, which was situated on the right lateral wall, in the cornu and slightly on the septum. Good recovery.

CASE 32. Age 24; primigravida.
This patient was the wife of an American soldier and was brought to me by her mother when she was 24 weeks pregnant. The patient wished to

join her husband in America and her mother wanted her to stay in England until the baby was born. The reason for this was that the mother had had "such terrible times with her babies" that she was convinced the same fate would befall her daughter. This idea was strengthened by the fact that her eldest daughter had lost her life in childbirth. The patient was 24 weeks pregnant with a very obvious uterine deformity and a transverse lie.

The mother was a communicative woman and told me that at each of her 11 labours she "had one foot in the grave and that she had sent her family doctor prematurely to his death by the worry of her repeated abnormal pregnancies." The latter part of this statement was the more regrettable, in that he was thus unable to give me valuable information about the true obstetric history of this woman. However, I did interview the handywoman who had attended some of her labours with the doctor and after a stern cross-examination in which I tried to eliminate all romancing it seemed likely that this woman had had placenta praevia on 3 occasions, postpartum haemorrhage on 4 others and one "turning-operation to bring the baby." I tried to persuade her to let me put lipiodol into her uterus but she refused. I obtained a copy of her eldest daughter's death certificate and the certified cause of death was "antepartum haemorrhage and shock due to placenta praevia—internal version". The doctor who signed this certificate is now also dead. It seems probable that the mother and both her daughters had this uterine deformity. I advised my patient to stay at home until she was delivered, but she refused my advice and went to America. I have tried to find out the outcome of her pregnancy, but I have not received replies to my letters and the mother is apparently so frightened that I will again suggest putting lipiodol into her uterus that she will not come to see me.

CASE 33. Age 23; primigravida.
Pregnancy 1. Repeated transverse lie throughout pregnancy. Version was attempted twice and malpresentation recurred each time. Labour at term and foetus remained transverse. Lower segment Caesarean section done. Living male child weighing 7 pounds. Placenta on right lateral wall and in right cornu.

CASE 34. Age 20; primigravida.
Pregnancy 1. Normal pregnancy and labour; vertex presentation. Placenta retained 2 hours with postpartum haemorrhage treated by manual removal. Placenta in left cornu.

CASE 35. Age 23; primigravida.
Pregnancy 1. Normal pregnancy; vertex presentation, persistent occipito-posterior. Manual rotation and forceps delivery at term. Third stage normal.

CASE 36. Age 27; primigravida.
Pregnancy 1. Normal pregnancy and labour, vertex presentation. Retained placenta with postpartum haemorrhage treated by manual removal. Placenta in right cornu.

CASE 37. Age 66; 1-para.
This patient was referred to me at the cancer clinic for postmenopausal haemorrhage. She had had one normal pregnancy and delivery. I found that the fundus of the uterus contained a carcinoma and I performed a panhysterectomy. The uterus proved to be a well-marked example of uterus bicornis unicorpus unicollis, with a pedunculated adenocarcinoma growing from the apex of the septum. No other part of the uterine wall was involved in the growth, which was the size of a walnut.

All the uteri in this series were of the variety which I designated uterus bicornis unicorpus unicollis. In the first series there were 5 cases of uterus subseptus and 5 of uterus bicornis unicorpus unicollis and 1 which it was impossible to classify accurately as only the shape of the cavity was known. In the whole series the classification is therefore:

Uterus bicornis unicorpus unicollis	31
Uterus subseptus	5
Unclassified	1
Total	37

Table I shows a summary of the 78 pregnancies of which details are known and Table II shows the type and number of abnormalities which occurred in these 78 pregnancies.

TABLE I.

Case	1	2	3	4	5	6
			Pregnancy			
1.	Transverse stillborn	Transverse placenta praevia	Transverse			
2.	Premature transverse to breech	Transverse presentation of cord Placenta praevia				
3.	Abortion	Normal delivery, retention of cotyledon of placenta	Normal delivery	Abortion	Transversed retained placenta	Normal Oblique to vertex (spontaneous)
4.	Abortion	Transverse Retained placenta				
5.	Premature vertex stillborn	Transverse prolapsed cord				
6.	Premature twins, both breech.	Forceps delivery	Twins Breech and foetus compressus	Breech		
7.	Transverse to vertex	Transverse				
8.	?	Transverse	Transverse			
9.	Abortion					
10.	Abortion	Transverse				
11.	Abortion	Abortion	Abortion	Abortion	Abortion	
12.	Abortion	Abortion				
13.	Transverse					
14.	Vertex					
15.	Vertex placenta praevia					
16.	Vertex	?	Abortion	Abortion	Abortion	Vertex
17.	Vertex					
18.	Vertex	Vertex	Premature vertex			
19.	Vertex	Breech P.P.H.				
20.	Transverse to vertex P.P.H.					
21.	Vertex	Transverse to vertex P.P.H.				
22.	Vertex	Premature Transverse Prolapsed cord retained placenta				
23.	Vertex P.P.H. retained placenta					

TABLE I (*Continued*)

Case	Pregnancy 1	2	3	4	5	6
24.	Abortion	Abortion	Vertex			
25.	Vertex	Breech	Breech	Vertex	Vertex	Transverse placenta praevia
26.	Vertex					
27.	Vertex	Transverse to breech Prolapsed cord				
28.	Premature vertex	Ectopic				
29.	Abortion	Transverse				
30.	Vertex	Transverse				
31.	Abortion	Vertex retained placenta P.P.H.				
32.	(Transverse)*					
33.	Transverse					
34.	Vertex retained placenta P.P.H.					
35.	Vertex					
36.	Vertex retained placenta P.P.H.					
37.	Vertex					

* At 24 weeks. Patient lost sight of and outcome unknown.
Case 7 and Case 30 were sisters.

TABLE II.
Complications of Pregnancy and Labour.

Number of patients, 37.
Number of pregnancies, 78.

Transverse lie	...	...	...	21 (27 per cent)
Abortion	...	...	...	19 (26 per cent)
Retained placenta	...	...	12 (15 per cent)
Breech	...	...	...	7 (9 per cent)
Premature labour	...	...	7 (9 per cent)
Placenta praevia	...	...	4 (5 per cent)
Prolapse of cord ...	...	...	4 (5 per cent)

As in my previous series transverse lie was the commonest abnormality seen in these cases. Some of them underwent spontaneous version even as late as the commencement of labour. It is obvious therefore that the routine employment of Caesarean section in these patients is unnecessary and is to be deprecated. I now allow the patient to go to term in every case. If the baby is very large or cannot be moved from the transverse by attempts at version then I perform Caesarean section at the onset of labour; in other cases I allow labour to proceed as spontaneous version often takes place in the first stage. If it does not, provided the membranes can be retained intact for long enough, internal version can be used as an alternative. As soon as the membranes rupture the patient must be examined vaginally. If the os is more than half dilated internal version is indicated. If it is not or the cord has prolapsed there should be a very strong contra-indication to deter the operator from performing Caesarean section.

In all these cases I perform examination under anaesthesia before attempting version, owing to the likelihood of meeting with placenta praevia.

Abortion.

There seems no reason to alter the remarks that I made in my previous paper. I urged the radiological examination of the uterus in cases of repeated abortion, and where the syndrome is definitely the result of the deformity operative correction is called for. This is perhaps the most difficult aspect of the subject upon which to give advice conscientiously. Two abortions or even 3 may be followed by an uneventful pregnancy. The operation is not an easy one and the risks of rupture of the scar in a subsequent pregnancy must be remembered, especially as the scar must of necessity be placed in a very unfavourable position, namely the uterine fundus.

Postpartum Haemorrhage.

In this second series (Cases 16 onwards) the greatest conservatism was practised in the conduct of the third stage. Despite this, retention of the placenta occurred in 9 cases and there was postpartum haemorrhage in 5. In 2 of these the haemorrhage was very severe. This was due to the reluctance of a junior medical officer to manually remove the placenta quickly enough. Conservatism is, of course, correct, but at the first sign of free bleeding there should be no delay in attempting Crede's manoeuvre and, if it fails, in following it immediately by manual removal.

I stated in my previous paper that all patients with this deformity should be delivered in hospital. One of the strongest reasons for this statement is the liability of these patients to develop difficulties in the third stage. Manual removal of the placenta is a serious operation even under ideal conditions. In domiciliary midwifery it is in the majority of cases positively dangerous. Since by palpation most of these cases can be recognized at antenatal examination there is no reason why they should not be admitted for their labour to a hospital where blood transfusion is available and asepsis and antisepsis easily achieved.

Placenta Praevia.

In the earlier series it seemed that this deformity favoured placenta praevia and this is supported by fresh evidence. A review of the literature reveals papers describing this deformity in women who had placenta praevia in successive pregnancies. Schwarz, in 1891, described such a patient who had 3 successive pregnancies with placenta praevia on each occasion. Fifty years later Andrews and Nicholls (1941) of Norfolk, U.S.A., described another case. Their patient suffered from placenta praevia in each of her 3 confinements. At the third she was delivered by Caesarean section. They describe the uterus as having a septum which projected into the cavity and a dimple on the external surface, but they do not seem to associate the deformity with the occurrence of the placenta praevia. The remainder of the literature, such as it is, on the subject of placenta praevia in repeated pregnancies makes no mention of uterine deformities nor is there any evidence to show that the authors ever looked for such a cause.

Prolapsed Cord.

It is not surprising that this complication should be seen since transverse lie (itself a condition predisposing to prolapsed cord) is seen so frequently. It is obviously a secondary effect of the deformity.

Inheritance of the Deformity.

Once again in this series I found a still-born offspring of one of the mothers to have a uterus bicornis unicorpus unicollis. In addition Case 7 and Case 30 were sisters, and in Case 32 it is likely that this patient's mother had the deformity and possibly also her elder sister.

Carcinoma of the Uterus.

The last case described was discovered accidentally at an operation for uterine carcinoma. The literature contains quite a number of such case reports and specimens of such are not infrequently seen in museums. It is possible that a great many of these cases find their way into museums because of their "specimen appeal" but it would be interesting to know if there is a true increase in the incidence of carcinoma in malformed uteri.

SUMMARY.

1. A further 19 cases of minor degrees of failure of fusion of the Müllerian ducts are described.

2. The details of 78 pregnancies are given.

3. The commonest complications observed were transverse lie (27 per cent), abortion (26 per cent) and retained placenta (15 per cent). The management of these is discussed.

4. A plea is made for the detection of these cases during the antenatal period and for their delivery in hospital.

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Angular Pregnancy at Term complicated by Constriction Ring

BY

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ANGULAR pregnancy progressing to term is a rare phenomenon (DeLee, 1940b; Kerr, 1944b).

Constriction ring is an uncommon complication of labour (Gibberd, 1938).

A combination of these conditions—if the diagnosis be correct—together with partial destruction of the affected uterine muscle and lipiodol leakage into the pelvic veins (when, during convalescence, attempts were made to demonstrate the remaining uterine cavity) makes this case sufficiently interesting to warrant publication.

Mrs. C. J., 27 years old, Cape coloured, 4-para, was admitted at 4 p.m. on July 11th, 1946, being sent into hospital by her doctor as a " Tonic contraction of the uterus."

History.

Past. 1932, aborted when 3 months pregnant. 1942, normal pregnancy, delivery and puerperium, at term. 1945, normal pregnancy, delivery and puerperium, at term. These deliveries took place at home. Both her children are alive.

Present. The patient states that she did not attend an antenatal clinic.

Up to July 4th, 1946, she was perfectly well and carried on with her household duties as usual. The following day she noticed that all foetal movements had ceased. On July 6th she experienced a dull backache and lower abdominal cramps, that is, like the onset of a normal labour. During the day her membranes ruptured. On July 7th she had slight infrequent, irregular labour pains. The pains passed off after about 12 hours. Towards evening she felt slightly feverish. Since July 8th she had had more or less continuous dull abdominal pain. At odd intervals a little blood escaped from her vagina. On the 10th dark evil-smelling " clots " were passed vaginally. Although she felt ill she was not confined to bed.

Since July 11th she had felt really ill, being more feverish than before. She was too ill to get out of bed. She now noticed small fine hair in the vaginal discharge. She sent for a doctor. He examined her vaginally and sent her into hospital.

On Examination.

General. The patient looked very ill. There were sordes on her lips and her tongue was dry. Temperature, 100.8°F.; pulse, 160; respirations, 35; blood-pressure, 115/90 mm.Hg.

Local.

Abdomen. The abdomen was grossly distended. The fundus was up to the ensiform cartilage. The uterus was tense and tender. No gut was felt lying anterior to the uterus. The lie of the child could not be determined. Palpation revealed a peculiar crackling sensation over the uterus. The uterus was resonant to percussion. The foetal heart was not heard.

Vaginal examination. There was a foul-smelling, bloody-purulent vaginal discharge. A swab was taken for bacteriological examination. The os admitted 2 fingers. Separating the os from the head was a cylindrical channel about 1½ inches long, admitting 1 finger only. The membranes were found to be ruptured and scalp was protruding through both the narrow channel and cervix. The head was presenting. Bare bone was palpated. The upper end of the constricted channel was tightly applied to the head. The head was pushed up in order to allow gas to escape. The gas was foul smelling. Foetal hair was present on the examining finger.

Urine. Orange colour, specific gravity, 1014; trace of albumen; no sugar or acetone.

X-ray (straight-portable), *vide* Fig. 1. Postero-anterior and lateral views taken to show the gas within the uterus.

Treatment. Antigasgangrene serum, penicillin, sulfadiazine, intravenous saliine and glucose followed by 2 pints whole blood given.

11 p.m. There was slight improvement in the clinical picture. There were no uterine contractions. Vaginal examination made to let out more gas. There was no change in the state of either the cervix or the ring.

July 12th, 1946. 3 a.m. The patient had a rigor. 5 a.m. Abdominal distension had increased. Vaginal examination made to release gas. There was no change either in cervix or ring. 6 a.m., castor oil 2 ounces per os; 8 a.m., hot enema; 10 a.m., pituitrin, m. 3 given intramuscularly, quinine gr. 1 per os; 11 a.m., 12 noon, 1 p.m., pituitrin and quinine repeated.

As there were no uterine contractions (objectively) and as the patient's condition now started deteriorating—her pulse-rate increasing with a severe drop in temperature—hysterectomy was decided upon.

The diagnosis was (1) Foetal death and putrefaction. (2) Paralysis or death of the uterine muscle. (3) Puerperal infection (? Gas gangrene).

Preliminary bacteriological report: "Large gram-positive bacilli present in fair numbers, various sizes, some filamentous, others tending to form chains. Few showing enlarged terminal spores."

Blood transfusion was started again in order to continue throughout and after the operation (3 pints were given). As it was not clear whether a subtotal could be done, the patient was prepared for a total hysterectomy.

Operation.

July 12th, 1946, 2 p.m. The vagina was cleared and the external os was stitched after a plug was inserted into the uterus. The abdomen was opened by means of a midline incision extending from 2 inches above the umbilicus to 1 inch above the symphysis pubis. On opening the abdomen omentum was found to be adherent to the fundus and anterior surface of the uterus. It was also adherent to the peritoneum of the anterior abdominal wall. The upper segment was greenish-purple in colour, extremely thin, and stank. The lower segment appeared normal. There was no clear line of demarcation. A subtotal hysterectomy was therefore decided upon. Omental adhesions were

stripped where possible and severed and tied where the latter was impossible When the anterior wall and fundal adhesions were cleared the uterus was lifted out of the abdominal cavity only to find that gut was adherent to its posterior wall. These adhesions were now freed. Once lifted out of the abdominal cavity the uterus was well packed off with swabs.

A subtotal hysterectomy was done in the usual way. The essential differences were that the vessels on the right side—both uterine and ovarian, were grossly enlarged. The lower segment was friable. In order to avoid intra-peritoneal spilling the lower segment was severed between clamps. The amputation was at a higher level than reached by the plug inserted before the abdominal operation. The uterine stump was covered with peritoneum. A drainage tube was inserted. The abdomen was closed in the usual way.

20 ml. prontosil rubrum were injected through the drainage tube. The stitches closing the external os were removed. The intracervical-uterine plug was removed. For photographs and description of the specimen see Figs. 2, 3 and 4.

On regaining consciousness after the anaesthetic the patient vomited "coffee grounds". A duodenal tube was immediately inserted; 1 pint was withdrawn. Continuous gastric suction apparatus was connected. The patient made a steady recovery.

Further bacteriological report:

Blood agar. Very light growth; scanty staphylococcus albus; viridans colonies of gram-positive cocci; scanty coliform bacilli.

Egg meat. Scanty long-chained streptococci only.

Milk under oil. Numerous long-chained streptococci. No gram-positive bacilli after 24 hours.

Serum broth. Gram-positive bacilli (? diphtheroids); gram-positive diplococci, some in chains.

No gas gangrene organisms isolated after 3 days. Viridans streptococci from milk and egg meat subcultures (aerobically).

After a total of 640,000 units penicillin and 17 grams sulfadiazine on July 18th, 1946, the patient's drug treatment ceased. Her wound healed by first intention. She was allowed up on July 24th after a vaginal examination which revealed an anteverted mobile uterus which corresponded in size to a normal uterus at this stage of involution. As the

patient would no longer stay in hospital a hysterogram was done on July 31st.

September 13th, 1946. She stated that she felt perfectly fit. She bled slightly after the lipiodol injection of July 31st, but not since.

On examination. Scar, well healed; *per vaginam*, cervix normal; uterus, could not be clearly defined.

Hysterogram done (see Fig. 5).

There was slight vaginal bleeding at the completion of the examination.

DISCUSSION.

From the history, clinical examination, photographs and legends, the following deductions may logically be made:

1. *Angular Pregnancy.*

Figs. 2, 3 and 4 show that the Fallopian tube, round ligament and ovary are attached high up on the right side of the specimen whereas the uterine attachment of the left adnexa is below the level of the head of the foetus, i.e., the left side of the uterus did not take any active part in this pregnancy.

Therefore, the ovum was implanted either in the right cornu of the uterus, in a diverticulum, in a rudimentary horn, in one cornu of a uterus bicornis, or in a sacculus.

Against a pregnancy in a diverticulum (Bennett, 1937; DeLee, 1940c; Hawkins, 1945; Stander, 1941c) rudimentary horn (Kerr, 1944a) or uterus bicornis (Corbet, 1945) is the fact that the uterus is not separate and distinct from the pregnancy.

Sacculation (DeLee, 1940a; Stander, 1941a) can be ruled out as there is no history of pain or urinary disturbances pointing toward a displaced uterus unable to correct itself.

The situation also is against sacculation as the latter tends to affect the anterior wall in retroflexions and the posterior wall following ventral suspensions (Stander, 1941b).

The pregnancy was completely within the uterus with the placenta attached to the area over the entry of the right Fallopian tube into the uterus. It thus conforms to angular pregnancy as described by Munro Kerr (1944b) and DeLee (1940b).

2. *Constriction Ring.*

Viewing Fig. 4 will show that:

(*a*) Clinically the os was found to be 2 fingers dilated. There was a narrow cylindrical uterine channel extending from the cervix (? plus lower part of the body of the uterus—as it easily admitted a swab—*vide* "operation") to the head of the foetus.

(*b*) Operatively the foetus was found to lie in what logically was a thinned-out cornu and fundus of the uterus.

The dilated os shows that the cervix took part in the labour. That this channel was not the original uterus below the angular pregnancy is borne out by the following facts:

(i) The cervix took an active part in the labour—a function not performed with ectopic pregnancy.

(ii) Had this channel been the original uterus it should have admitted more than one finger as the uterus enlarged, due to hormonal influence, no matter where the pregnancy is situated.

Therefore it can be assumed that this ring-like channel was due to a segment of uterine muscle in spasm, i.e., a constriction ring, the site of the ring being at the junction of the affected cornu plus fundus with the body of the uterus.

The situation, embryologically, tends to favour Rudolph's (1935) theory on the aetiology of constriction ring, that is, at sites of physiological constrictions found in lower animals.

3. *Physometria.*

Both clinically—the uterus being resonant to percussion and because of the escape

of gas from the uterus when the foetal head was pushed up—and radiologically (Fig. 1) the diagnosis of physometria was established.
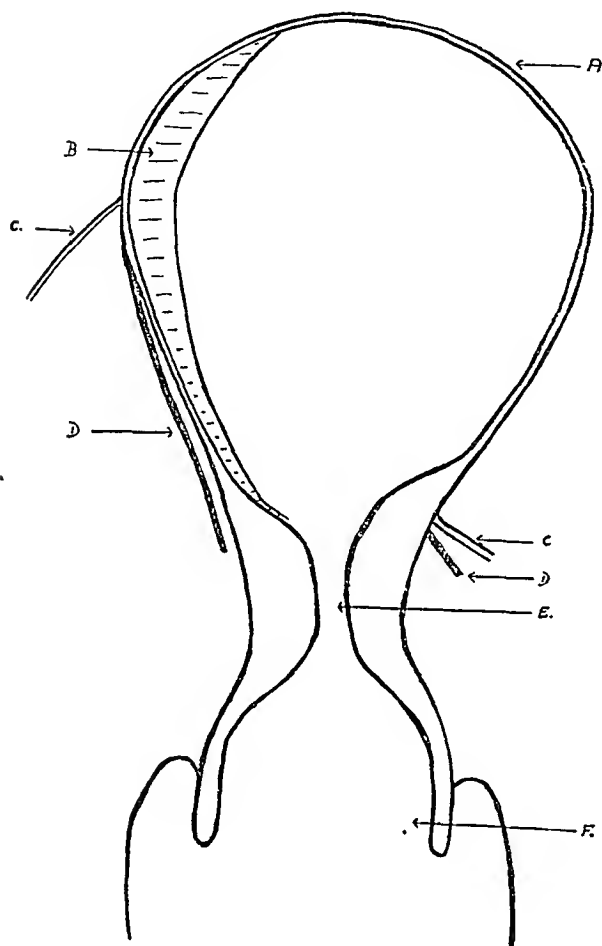
FIG. 4

Sketch of combined operative and clinical picture.

A. Thinned wall of the uterus.
B. Placenta.
C. Fallopian tube.
D. Round ligament.
E. Narrow lumen surrounded by
   thick uterine muscle.
F. Cervix—2 fingers dilated.

4. *Partial Destruction.*

This can be seen by studying Figs. 2 and 3. The following argument explains the course of the partial destruction.

The history suggests death of the foetus before the onset of the poor type of labour, that is, complete absence of foetal movement. The membranes ruptured early in labour.

At the onset of, or during, labour the constriction ring developed. (Vaginal bleeding occurred 4 days after the onset of abdominal cramps. Fig. 3 shows the placenta extending on to the ring. This suggests that the placenta acted "praevia" after the formation of the cervix-like ring.)

The amniotic cavity· became infected, the foetus macerated. Foetal scalp sloughed, plugged the constriction ring, and prevented the escape of both infected fluid and gas. The tension within the pregnant sac increased.

According to Morison and Saint (1935) an increase in tension diminishes or cuts off the blood supply to the affected part. This in turn leads to partial destruction. Hence the gangrenous macroscopic appearance of the muscle surrounding the foetus (Fig. 2). This was confirmed histologically.

5. *Recovery.*

The patient's recovery is a remarkable feat. Her resistance, penicillin, sulpha drugs, adequate fluid balance, blood transfusions and nursing can be claimed as the responsible factors.

6. *Lipiodol in Pelvic Veins.*

In order to prove beyond doubt that the major part of the body of the uterus was still left a hysterogram was done 20 days after her operation. It was done so soon post-operatively for fear of losing sight of the patient as she threatened to sign "the red ticket and quit hospital."

The uterine cavity was poorly outlined. Lipiodol intravasation occurred into the pelvic veins. Six weeks later she returned to the out-patient department. Lipiodol again was gently injected through the cervix. Fig. 5 shows the result, again it·
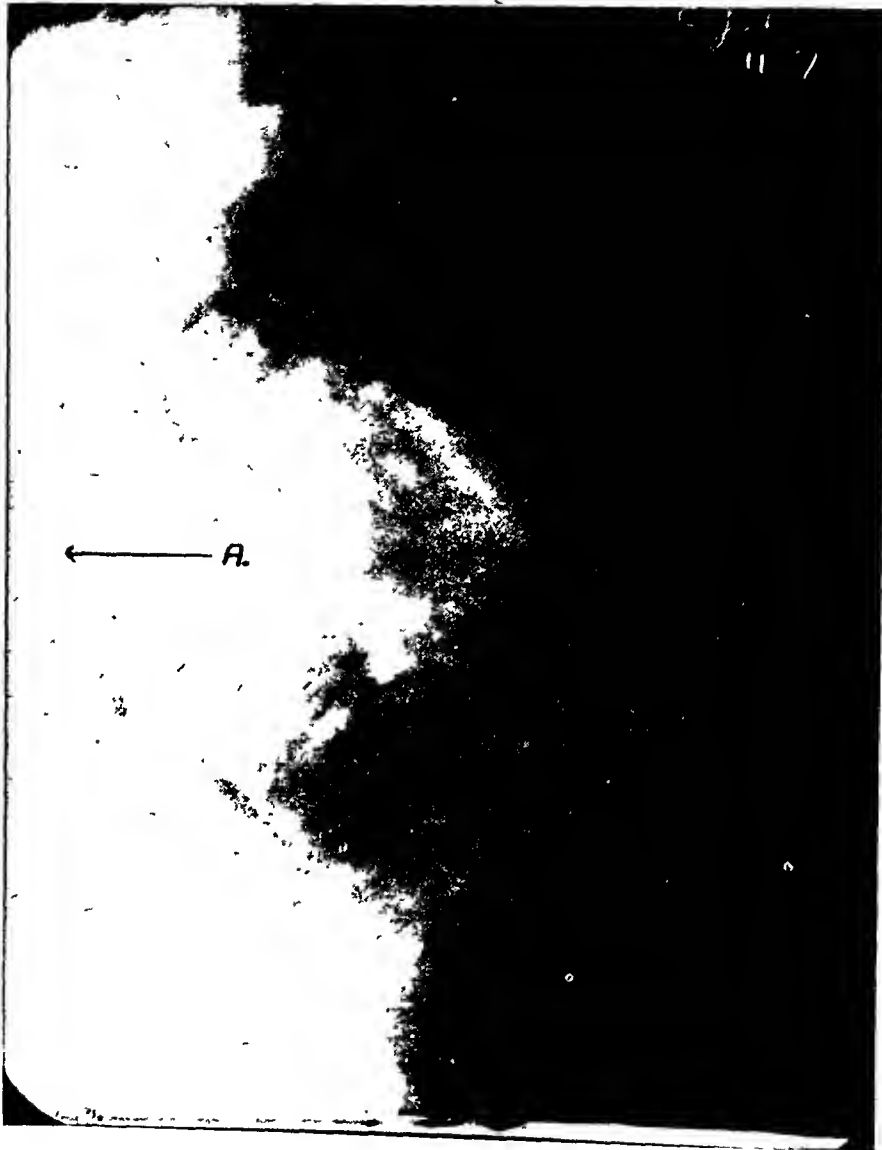
Fig. 1

Lateral view of abdomen (Portable).
A. Gas between foetus and uterus wall.

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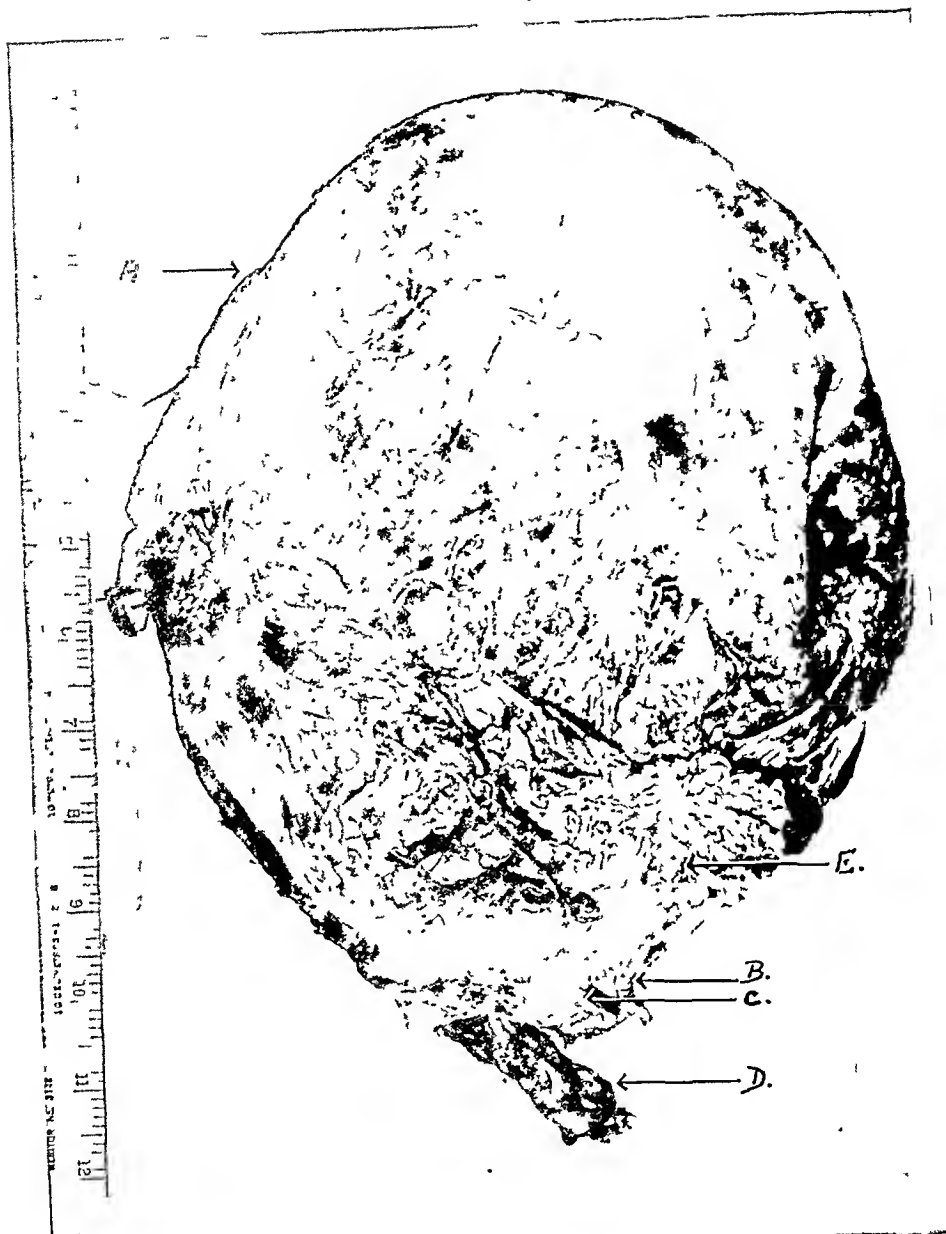
FIG. 2

Anterior view of specimen

A. Insertion of right Fallopian tube.   B Left Fallopian tube.
C. Left round ligament   D. Scalp protruding.
E. Omental adhesion.

J. T. L.

FIG. 3

Specimen opened.

A. Macerated foetus.   B. Thin walled " uterus ".
C. Thick " ring " locking in the foetus.
D. Scalp protruding through the ring.
E. Placenta attached down on the thick rim (on the left side).

J. T. L.
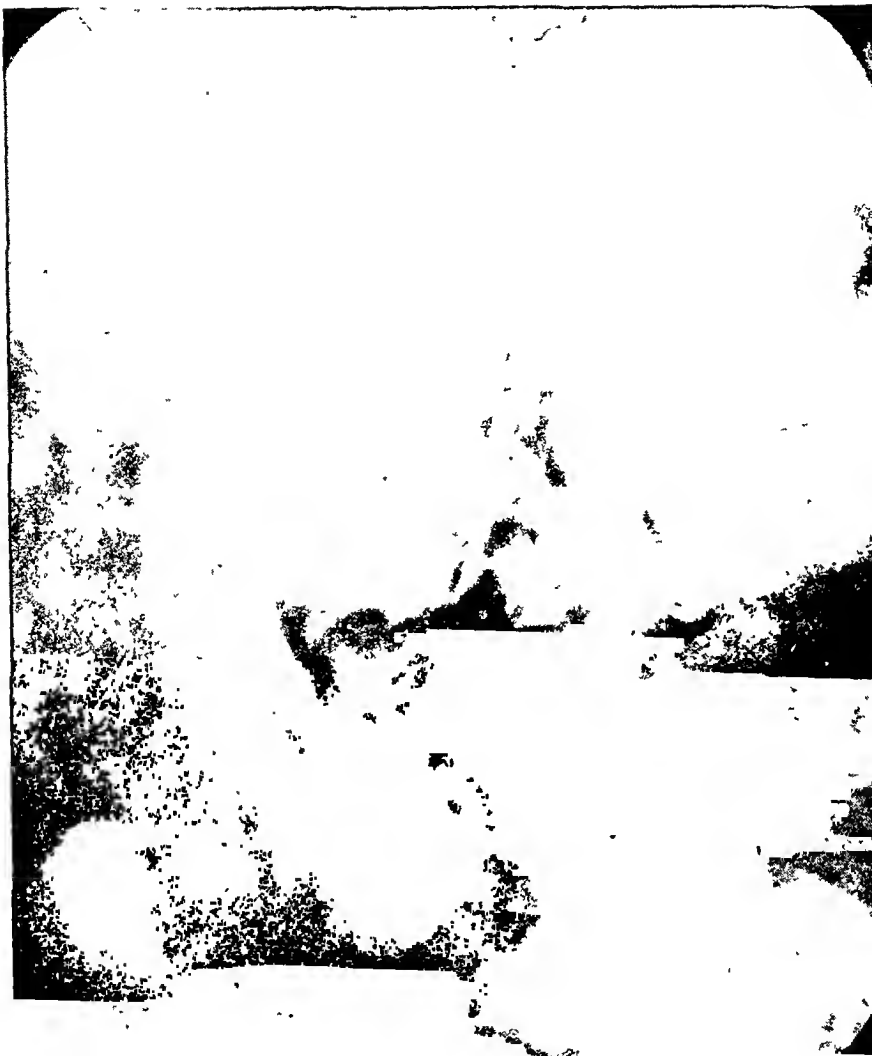
FIG. 5

Lipiodol leaked from the uterine cavity into the pelvic venous plexus markedly on the right side.

J. T. L.

escaped into the pelvic veins. The veinous intravasation of lipiodol is a rare phenomenon (Bloomfield, 1946; Roblee and Moore, 1945). The patient has failed to report for further examination.

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The Effect of Methyl-Ergometrine on the Human Puerperal Uterus

BY

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THE isolation of ergometrine in 1935 provided a drug which rapidly superseded ergotamine and ergotoxine in obstetric practice, and became recognized as being the oxytocic drug of choice during the post-partum period. Its advantages were greater potency, more rapid action, and absence of undesirable side-effects, in particular gangrene of the extremities.

The use of ergot preparations is generally considered to be contra-indicated before the end of the third stage of labour, because of the prolonged nature of the uterine response produced, but some workers, particularly in the United States and in continental Europe, have recently recommended the wider use of ergometrine. In particular, several authors (O'Connor, 1944; McConnell and Schauffler, 1943) have reported very favourably on the practice of giving the drug intravenously as the anterior shoulder appears under the pubic arch. It has also been used in uterine inertia and to induce labour, but these indications are not regarded with favour in this country because of the danger of foetal asphyxia. As an emergency measure, its administration is recommended by many obstetricians (Flew *et al.*, 1947; Moir, 1944a) for haemorrhage, associated with a relaxed uterus, occurring during the third stage of labour.

For a drug to supersede ergometrine it must at least equal that alkaloid in the qualities described, and should possess some further advantage. In 1943 Stoll and Hoffman introduced methyl-ergometrine, at first known as ME 277, and later given the commercial name of "Methergine". This substance was claimed to have all the virtues of ergometrine, to be equally free from unpleasant side-effects and to be rather more powerful.

Chemistry.

Chemically, the drug is *d*-lysergic acid butanol 2-amide tartarate. From the manufacturing point of view it has considerable advantages over ergometrine.

The yield of pure ergometrine from crude ergot is very small indeed and varies considerably from one sample to another; it is economical to extract only the better grades of ergot, and these must be imported, mainly from Spain. All the alkaloids of ergot contain in their molecular structure a complex organic acid, *d*-lysergic acid, which is itself pharmacologically inert. In any sample of ergot there are a large number of alkaloids, most of which are, however, pharmacologically inert or of little clinical value. In the preparation of methyl-ergometrine this mixture of alkaloids is broken down; the *d*-lysergic acid is extracted, and from it methyl-ergometrine is synthesized. By this means the total yield of methyl-ergometrine is of the order of eight times that of ergometrine and, as it is apparently more potent, the effective yield is greater still. Furthermore, the cruder samples of ergot may be utilized.

Pharmacology.

During the recent war methyl-ergometrine was manufactured and marketed in Switzerland and in the United States, but it has only recently become available in Great Britain. A number of reports have already been published dealing with its pharmacology and some aspects of its clinical application. Kirchof *et al* (1944) have demonstrated that it exerts a powerful oxytocic effect in the rabbit and guinea-pig. They found no evidence of toxicity in humans. They concluded that the oxytocic effect was at least equal to that of ergometrine. Bachbauer (1944) investigated tokometrically the effect on human uterine contractions during pregnancy, labour and the puerperium, and considered that its properties were similar to those of ergometrine. The drug appears to be free from the sympathicolytic effects of ergotamine and ergotoxine.

Clinical Reports.

Brougher (1945) administered the drug in doses of 0.2 mg. to 288 women as the foetal shoulder was born, and compared his results with a control series of patients to whom ergometrine was given in a similar way. The blood loss was about equal. In 3 patients manual removal of the placenta was necessary because of a contraction ring, which he attributed to delay in entering the vein whilst giving the injection. A uterine contraction occurred 20 to 30 seconds after intravenous administration, and this contraction was maintained longer in the methyl-ergometrine series.

Tollefson (1944) gave doses of 0.2 mg. to 200 patients as soon as the placenta was thought to have separated. A uterine contraction followed on an average in 48 seconds and the placenta was then expressed; there was little blood loss, but he noted an increase in after pains. In 12 cases, however, it was given before the placenta had fully separated, and the resultant contraction lasted 1 to 2 hours. Cartwright and Rogers (1946), Roberts (1944), Tritsch and Schneider (1945), Janke (1942), and d'Ernst (1946) have similarly reported that they have found it to be a highly efficient oxytocic during and after the third stage of labour.

The drug has also been given orally in dilute solution under the name of *Partergin,* and this has been used by Farber (1946) with success in the induction of labour, whilst Brunner (1946) has reported favourably on its effect in uterine inertia. However, the use of an oxytocic drug derived from ergot is potentially dangerous to the foetus as, if even moderate doses are given, there is a prolonged tense contraction of the uterus which is liable to lead to foetal asphyxia. In these experiments only very small doses were used, but even so it seems unlikely that such methods will be popular in this country. Moir (personal communication) recalls 2 cases in which ergometrine was used and an unexplained foetal death occurred. He believes that the deaths were due to foetal asphyxia associated with a degree of tonic contraction of the uterus.

THE PRESENT INVESTIGATION.

From the results of the work already published there seems little doubt that methyl-ergometrine is, from a clinical point of view, an efficient oxytocic drug and that it is apparently free from toxic effects. But a satisfactory comparison of the effects of ergometrine and methyl-ergometrine on the human uterus has not yet been published. The present investigation was undertaken in an attempt to provide such a comparison.

The technique using an intrauterine bag was adopted, the details of which have already been fully described (Moir, 1944b). In all some 24 tracings were made during the investigation.

As a standard for comparison, a series of tracings were made of the effect of the intravenous injection of 0.1 mg. of ergometrine in normal patients between the 6th and 8th days after delivery. The drug given was ergometrine maleate, but the dosage was calculated as 0.1 mg. of ergometrine alkaloid. Two typical tracings are shown in Fig. 1(a) and (b).

curve gradually returns to the original level in about 50 to 55 minutes, after which a series of rhythmical contractions follow at gradually lengthening intervals. These slowly merge into the normal puerperal waves, but last for several hours.

Methyl-ergometrine was then given to a similar series of patients. The dosages employed were all calculated as methyl-
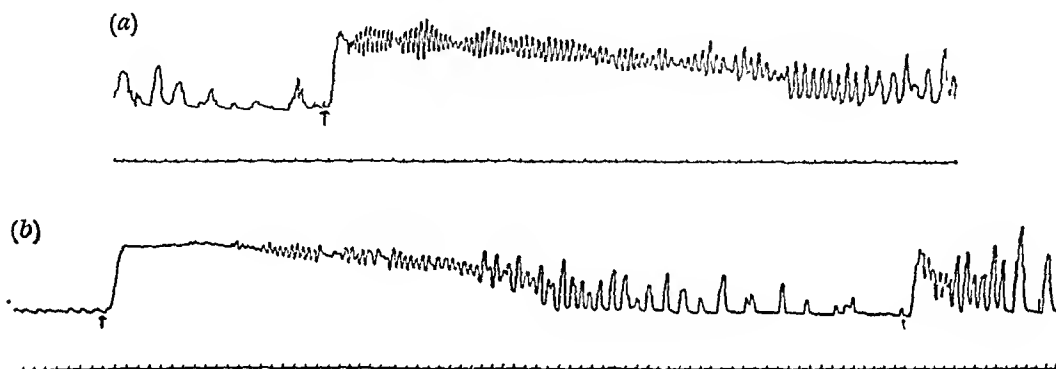
FIG. 1.

Intravenous injections of 0.1 mg. of ergometrine at ↑ . In (b) this dose was repeated after an interval of 1 hour 15 minutes, the second response being quite different from the first.

The time markings are minutes.

The effect of an intravenous injection of ergometrine on the 6th to 8th day of the puerperium has been fully described by Dudley and Moir (1935). The tracings in the present series confirm their findings.

Prior to the injection, the uterus may or may not show rhythmical contractions, generally of low amplitude. Following the injection there is a delay of rather less than a minute followed by a sharp, strong contraction. The delay in this series averaged 55 seconds and varied between 35 seconds and 78 seconds. This is slightly longer than is usually reported (Moir, 1936).

Following the initial rise, the uterus usually remains firmly contracted for a few minutes (this period varies from about 1 to 5 minutes) and then partially relaxes, the plateau giving way to a series of small contractions which increase in amplitude. The

ergometrine-tartarate, as the preparation was received in ampoules containing 0.2 mg. of this salt. Calculated on the basis of molecular concentration, a dosage of 0.145 mg. of methyl-ergometrine-tartarate is equivalent to a dosage of 0.1 mg. of ergometrine alkaloid. A dosage of 0.1 mg. was found to be a satisfactory dose for purposes of comparison. A series of tracings were made following the intravenous injection of this dose, 2 typical examples of such tracings being shown in Fig. 2(a) and (b). Tracings were also made following smaller doses (Fig. 3) showing the effect of a dosage in molecular concentration equivalent to 0.05 mg. of ergometrine alkaloid. In addition, tracings were taken following the administration of the drug intramuscularly (Fig. 4) and by mouth (Fig. 5). Finally, the drug was

(a)

(b)
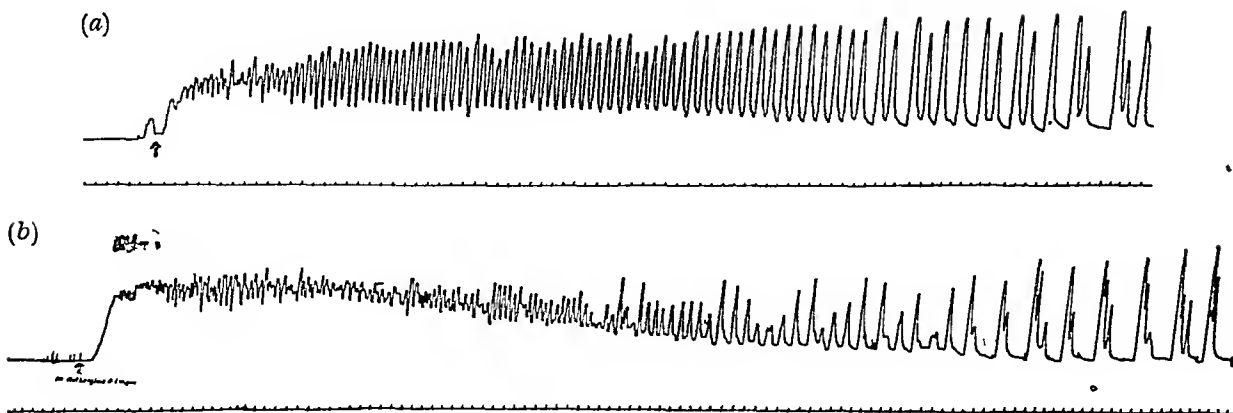
FIG. 2.

Intravenous injection of o.1 mg. of methyl-ergometrine-tartrate at ↑ .
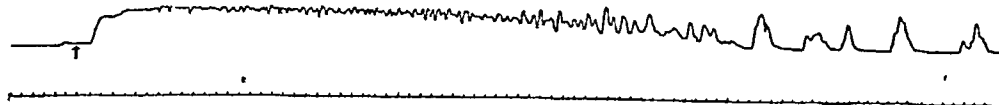
FIG. 3.

Intravenous injection of 0.072 mg. of methyl-ergometrine-tartarate at ↑ .

FIG. 4.

Intramuscular injection of o.1 mg. of methyl-ergometrine-tartrate at ↑ .
Delay of 9½ minutes.
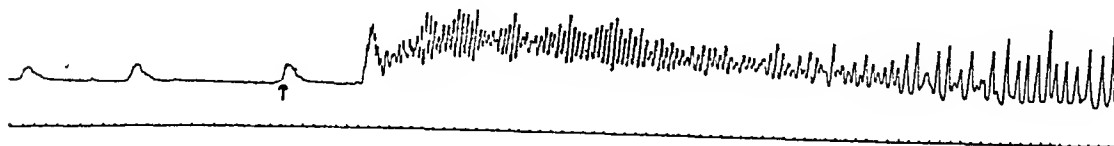
FIG. 5.

Methyl-ergometrine-tartarate 0.2 mg. was given by mouth at ↑ . Delay of
7 minutes.

used clinically in a very small series of patients; o.2 mg. of methyl-ergometrine-tartarate was given intravenously shortly after delivery of the placenta, whilst the uterus was relaxed. The delay before a firm uterine contraction could be palpated was noted; such a measurement is, of course, merely an impression and is not absolutely accurate and, furthermore, it is impossible to be certain whether the contraction felt is due to the effect of the drug or is spontaneous.

Unfortunately, it is not practicable to compare the effect of the two drugs on the same uterus on the same day. After an injection of either drug during the puer-

perium, the normal contractions of the uterus are hyperactive for some hours; also for several hours the uterus is left in a relatively refractory state to a further dose of either oxytocic. An example of this is Fig. 1(b), which shows the effect of 2 injections of 0.1 mg. of ergometrine, with an interval of $1\frac{1}{4}$ hours. Furthermore, to maintain a continuous record for more than about 3 hours is impracticable because of suckling, movement of the patient, the state of the bladder and rectum and other factors. However, the findings over a series of tracings proved sufficiently constant for an accurate comparison to be made.

Comparison of Tracings.

Qualitatively, the tracings following intravenous administration of the two drugs are very similar. Quantitatively, however, there are definite differences, and a comparison was made between the ergometrine series (0.1 mg. of alkaloid) and the tracings taken after methyl-ergometrine-tartarate (0.1 mg.). In both series the drug was administered intravenously.

The Time of Onset.

After methyl-ergometrine there was an appreciably longer delay before the initial rise in the tracing, and this period was rather longer than that reported by Brougher (1945) and other workers. The average delay was 1 minute 36 seconds, the longest period being 2 minutes 20 seconds and the shortest 50 seconds. As mentioned earlier, the average delay following ergometrine was 55 seconds. Thus it would appear that ergometrine acts more rapidly, the difference being of the order of 40 seconds.

Nature of Contractions.

The type and sequence of contractions were identical in the two series. As with the previous drug, following the injection of methyl-ergometrine, there was a sharp initial rise, usually followed by a short plateau, which in turn gave place to a series of rhythmical contractions. At about the time that the tracing returned to the baseline, the contractions became intermittent and over a period of hours gradually merged into the normal puerperal rhythm. Fig. 2(b) shows the effect of methyl-ergometrine for 1 hour 45 minutes; and recordings for over 2 hours were similar. In general, the amplitude of the contractions was considerably greater after methyl-ergometrine, though individual variations were considerable. The frequency of the contractions was much the same for the two drugs.

The Base-line

The rise in the base-line represents uterine tonus and this can be measured accurately. There was a slightly greater rise after methyl-ergometrine, the ratio being 5:4. The duration of the rise was also measured and, in the methyl-ergometrine series, this averaged 72 minutes, whilst after ergometrine it averaged 54 minutes.

Side Effects.

In no case was any toxic effect noted after the administration of methyl-ergometrine, but no attempt was made to record the effect, if any, on the pulse-rate and blood-pressure. After-pains were reproduced in all patients who had already suffered from them early in the puerperium, and in one other case. They were transient and not severe. In 3 cases retained membranes were expelled.

Intramuscular Injection.

Methyl-ergometrine was administered by this route in 2 cases and the response was disappointing. The onset of the contractions was a gradual one, commencing 7 to 10 minutes after the injection. The estab-

lished contractions and the uterine tonus, were less marked than when it was given by mouth or intravenous injection. D'Ernst (1946) noted clinically that the response following intramuscular injection was unreliable. It would be necessary, however, to conduct a larger series of experiments before definitely stating that the response is consistently poor following intramuscular injection.

Oral Administration.

The drug was given orally in 1 case (Fig. 5). There was a delay of 7 minutes, after which, excepting for a less dramatic onset, the tracing was similar to those which followed intravenous injection. This is very similar to the effect of ergometrine by mouth, which has already been described by Moir (1936).

Use Immediately after Labour.

A few cases were observed in which methyl-ergometrine was given immediately after labour and the effect observed by palpating the uterus. On each occasion a firm uterine contraction was apparent within 70 seconds, usually in about 45 seconds. This agrees with the findings of Janke (1942) and Tollefson (1944). This latent period was shorter than that previously observed in the tracings (6th to 8th day of the puerperium), but a more extensive trial would be necessary to determine whether this difference in the speed of action between the very early and later puerperium is a constant feature of the drug.

DISCUSSION.

From a comparison of these tracings, there is no doubt that methyl-ergometrine exerts a powerful oxytocic effect on the human uterus on the 6th to 8th day of the puerperium. This effect is rapid in onset,

averaging 96 seconds after intravenous injection; this is 40 to 50 seconds longer than after a similar injection of ergometrine. This latent period in the puerperal uterus is longer than that previously reported as a result of clinical trials during and immediately after labour.

The effect is a powerful one, being rather more than 1.5 times as strong as with ergometrine when doses of equal molecular strength are compared. Thus, a dose of 0.2 mg. of methyl-ergometrine-tartarate is roughly equal in effect to a dose of 0.25 mg. of ergometrine alkaloid. The duration of the contractions is rather longer, the ratio being of the order of 4:3. Qualitatively, the drugs are almost identical. Methyl-ergometrine appears to be free from toxic effects. Theoretically the extra delay is a slight disadvantage, at least in cases of severe haemorrhage, but the blood loss in 40 seconds would not be very great and may to some extent be offset by the more prolonged oxytocic effect. This appears to be the only point in which it is inferior to ergometrine. Certainly the drug is worthy of an extensive clinical trial.

SUMMARY.

1. Methyl-ergometrine ("Methergine"), a new semi-synthetic ergot alkaloid, is described.

2. The effect of ergometrine and of methyl-ergometrine on the human puerperal uterus is compared.

3. Methyl-ergometrine is a powerful oxytocic drug, free from undesirable side-effects, with properties which closely resemble those of ergometrine.

4. As an oxytocic, methyl-ergometrine is, weight for weight, between 1.5 times and twice as powerful as ergometrine.

5. When methyl-ergometrine is administered intravenously, on the 6th to 8th day of the puerperium, the delay before the

uterus contracts is slightly greater than with ergometrine.

6. Weight for weight, methyl-ergometrine exerts a slightly more prolonged effect on the uterus than does ergometrine.

7. Methyl-ergometrine is effective when given by intravenous injection or by mouth; but the onset appears to be slower, and the contractions are less marked, if it is administered by the intramuscular route.

ACKNOWLEDGEMENTS.

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The Antenatal and Postnatal Care of the Erythroblastotic Infant[*]

BY

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THE problem of the erythroblastotic infant is one which, although not of everyday occurrence, is met with sufficiently often to warrant the adoption of a proper scheme of treatment. Such a scheme should be based on the underlying scientific principles involved in the aetiology of the condition. The incidence of erythroblastosis is approximately 1 in 300 of all pregnancies (Haldane, 1942; Whitby and Britton, 1946a): for comparison it is rather more common than face presentation, which occurs about 1 in every 300 labours. The number actually treated in obstetric centres will be greater than this because of those referred from domiciliary cases and nursing homes as being in need of special treatment. The state of many such infants, upon their arrival in hospital, makes it obvious that adequate treatment is, as yet, available only in a few specialized centres. When it is remembered that the mortality of untreated cases of erythroblastosis foetalis ranges from 50 to 80 per cent and that as high as 10 per cent of the cases which recover may be affected by central nervous system lesions (Hawksley and Lightwood, 1934; McKinley, 1941) or hepatosplenomegaly (Drummond and Watkins, 1946), it is highly desirable that such cases should be anticipated whenever possible, so that adequate treatment is available when required.

An extensive literature has already accumulated on the subject of erythroblastosis. This year there have been more than 90 publications on the subject to date, ranging geographically from Iceland to New Zealand, and in subject matter from complex genetic theories, such as that expounded by Fisher and Race (1946), to simple case reports (Venters, 1946). As yet however, there has been no attempt to apply the genetical and serological evidence to the formation of a practical guide for the treatment of affected cases. This paper is an attempt to fill this gap, until such time as a more comprehensive knowledge of the subject will dictate a more complete method of management.

It is based not only on the study of almost a score of cases occurring in the Jessop Hospital for Women during the last 12 months, each of which was as fully investigated as our knowledge at that time allowed, but also on an extensive use of the records of the National Blood Transfusion Service Sheffield Regional Laboratory, with whom we work in close co-operation.

THE ANTENATAL CARE.

In the first place erythroblastosis should be "anticipated". The word "anticipated" is used advisedly, as infants who will be affected can generally be detected before birth. A note of the routine procedure to discover these cases is given here.

All women at their first visit to the antenatal clinic should have blood taken for blood grouping, rhesus typing and a serological test for syphilis. If found to be Rh positive, as 85 per cent of women are, further investigation need not be made. If the woman is Rh negative and primigravid, further steps need not be taken

until the the eighth month. At the Sheffield Regional Transfusion Service Laboratory over 1,000 Rh negative primiparae had this first blood specimen tested for atypical agglutinins, with completely negative results. Because of this, tests for atypical agglutinins have been discontinued at this stage. At the eighth month, however, the blood should be again examined to confirm the Rh typing, and tested for atypical agglutinins in the serum. In most cases the result will again be negative, although a French paper (Hoet, de Somer and Vandenbroucke, 1946) reports an investigation into 60 families with erythroblastotic babies in which antibodies were found in the mother's serum in 8 cases of icterus in first-born children. These figures are so at variance with the findings of other workers, however, that they should be treated with great reserve.

In Rh negative multiparae, without a history suggestive of previous trouble, atypical agglutinins should be searched for at least once before the eighth month of pregnancy. It must also be remembered that a previous transfusion may have produced the same effect as a "sensitizing pregnancy", and this must be borne in mind until we know that there are no hospitals where a female child or woman of child-bearing age, is transfused before the rhesus typing has been determined. In an emergency Rh negative blood should be used. Once atypical agglutinins are discovered their titre should be determined and re-determined each month until delivery.

Even more care should be exercised in the supervision of multiparae with a definite history of children affected by erythroblastosis foetalis. The serum should be tested for agglutinins monthly throughout pregnancy, even though such tests may give negative results. On each occasion the tests should include not only those for the complete agglutinins, but also the Coombs' test (Coombs, Mourant and Race, 1945) for the incomplete or "blocking" antibody. This may sound like a great deal of investigation but it is not suggested without reason.

There is little doubt now that premature interruption of pregnancy is of value in properly selected cases. The foetus is removed from its harmful environment before the mother's antibodies have had time to complete the damage which they cause. However, following a careful study of all the case records available, one cannot but agree with the statement by Whitby and Britton (1946b), that "the titre of the anti-Rh antibodies in the mother is no criterion of the severity of the disease in the foetus." Nevertheless, this may be an apparent finding and not a truly accurate one. The number of such cases published, where the behaviour of the titre of the antibodies during the whole pregnancy is known, are very few. The statement that "the titre of the anti-Rh antibodies in the mother just before term is no criterion of the severity of the disease in the foetus" may be more accurate. Because of this the routine monthly testing of known or suspicious cases is advocated, for only when a large series of serological findings is finally correlated with the clinical results can a final verdict be passed.

An example of the apparently anomalous results so far obtained, but one which may fit into the scheme when a sufficient number of cases have been properly investigated, is quoted below:

Mrs. O., 3rd gravida.

First pregnancy in 1940, a mature female child weighing 7 pounds 3 ounces was born alive by natural forces. There was a history of jaundice shortly after birth, but the child is now alive and well.

Second pregnancy in 1944, a premature male

infant weighing 6 pounds 15 ounces was born at the 36th week. Delivery was normal. The infant died deeply jaundiced on the 5th day.

The husband was then found to be Rh positive —homozygous.

Third pregnancy—confinement due June 13th, 1946. At the seventh week her serum showed " Anti-Rh present in moderate strength ". At the 11th and 15th weeks " atypical agglutinin, presumably anti-Rh, still demonstrable at a very weak titre " was reported. At the 19th, 23rd and 28th weeks " no atypical agglutinin demonstrable at room or incubator temperature, and no incomplete antibody by the Weiner technique " was reported.

Three days after the last test a stillborn hydropic infant was delivered at 28 weeks, and 8 days later anti-Rh was demonstrable in the form of the incomplete anti-D variety.

This is perhaps an extreme example of the point I wish to make. Had this patient not been tested from her first appearance it would have been said that her serum gave no indication of trouble, because the presence of anti-Rh so early in the pregnancy would have been missed.

METHOD OF DELIVERY.

When complete records of a larger series of cases are available, fluctuations in the titre of the maternal antibodies may afford an indication of the severity of the disease in the foetus, and even dictate when to interfere; but at the moment, in the absence of such guidance, there is no doubt that the decision to perform Caesarean section or induction of labour must be made on the history. There are only two exceptions to this working rule which I can call to mind. Firstly, in the case where, on the history, trouble is considered inevitable, and yet, from the beginning of the pregnancy the routine serum tests all give negative results. Here the husband must be genotyped, as it is possible that he may be heterozygous. His wife may have carried 2 or 3 Rh positive children, but this particular one may be Rh negative and therefore unaffected. Obviously interference in such a case is completely unwarranted. In this respect it has been proved that there is a preponderance of homozygous fathers (Taylor and Race, 1944). I have been unable to find any case reported of an Rh negative woman, who has previously been sensitized to Rh positive antigen, carrying another Rh positive child without producing further antibodies.

Secondly, before performing Caesarean section, the foetus must always be X-rayed, not only to exclude the usual foetal abnormalities, but on rare occasions hydrops may be detected—the so-called Javert's sign (Javert, 1942)—in which case operation is, of course, contra-indicated.

Caesarean section is usually chosen as the method of terminating the pregnancy for 3 reasons. Firstly—these infants stand the strain of labour badly; not only because of their anaemic condition, but because of their increased tendency to bleed, which will be referred to shortly. The passage of a premature head through the pelvis, in an infant with a known predisposition to haemorrhage, is not desirable. Secondly, according to Javert (1942), another of the complications of labour in these cases is premature separation of an oedematous placenta. Interesting in this connexion is the observation that in cases of accidental haemorrhage the incidence of Rh negative women is higher than the normal 15 per cent. Thirdly, of course, there are the usual risks attendant upon the induction of premature labour in any case. In spite of these points, I think that in the case of a multipara with a normal pelvis, who has a vertex presentation, and has been allowed to continue beyond the 36th week of the pregnancy, surgical induction without rupture of the membranes is sometimes indicated.

During the last week, whilst preparing this paper, a most instructive case of a nature hitherto unreported has occurred.

An Rh negative woman (Mrs. A.) had 2 children, both Rh positive, genotype R_1r, the second of which suffered from icterus gravis neonatorum. Her husband was Rh positive but heterozygous. During her third pregnancy she was kept under close observation, and at the 35th week incomplete antibody was detected for the first time. Two weeks later this was much stronger at a titre of 1 in 32. In view of the past history and the fact that the incomplete antibody is believed to be the most pathogenic one (Cappel, 1946), labour was induced at the 38th week. Blood was given to the baby through the cord after delivery. It was found subsequently that the infant was Rh negative and unaffected.

The explanation of this apparent anomaly lies almost certainly in the fact that the third pregnancy afforded a non-specific stimulus, resulting in the reappearance of atypical agglutinins originally evoked by the second foetus. This problem had not previously been encountered, and it is suggested that in cases such as these, where the father is heterozygous and atypical agglutinins appear in the maternal circulation before delivery, preparation should be made to transfuse the infant after delivery, but the decision as to whether this should be done should be delayed until its necessity is demonstrated by a simple haemoglobin and red cell count. If this is done immediately upon birth the result can be known whilst the cord vessels are still available for transfusion purposes.

TREATMENT OF THE CHILD.

The tendency of the erythroblastotic infant to haemorrhage has already been mentioned. Authorities differ as to the reason for this, some attributing it to a low blood prothrombin level (Dam, Tage-Hansen and Plum, 1939), and others to a deficient number of platelets (Wiener and Wexler, 1943). Whatever the reason, there is little doubt that the tendency can be favourably influenced by the administration of vitamin K. Ideally it should be given, not to the infant after delivery, but to the mother before delivery. It has even been suggested that all Rh negative blood donors should be given adequate doses of vitamin K before donating blood, so that any Rh negative blood used in the treatment of jaundiced infants would have its full prothrombin content. This paper being concerned primarily with treatment, 2 small practical points of vitamin K therapy may be mentioned. It is effective if given to the mother as little as 4 hours before delivery. If given orally, bile salts should be given at the same time to break up the fat vehicle and obtain maximum absorption. When given to the infant, preferably intramuscularly to get the most rapid effect, a water soluble preparation is recommended, since an oily solution inevitably leads to a certain number of abscesses at the injection sites, however careful the asceptic technique. Since changing to the watery solution further complications of this nature have not been encountered.

Therapy with vitamin K is not the sole prophylactic treatment for haemorrhage. All affected infants should be treated with the same respect as is shown to a breech delivery, and kept quietly in the nursery for some days. Unheralded cerebral haemorrhage on the third day has been known to occur with a normal vertex delivery from a 2nd gravida and has been subsequently confirmed postmortem.

Turning to the subject of transfusion, there is general agreement that the transfusion of compatible Rh negative blood is the most effective treatment for this condition. There has been, as yet, little attempt to say when, how and how much to give. A study of the haemoglobin percentage

and the red blood cell count of our cases by graphing the results on a logarithmic scale, coupled with examination of the blood films, has encouraged the formation of certain tentative opinions. Mention of these may serve to stimulate other investigators.

From this point one must assume that not all cases have come from one's own antenatal clinic and therefore have not been "anticipated". Indeed the question of diagnosis may arise. A discussion into the differential diagnosis of jaundice in the newborn would be out of place in this paper, but one pitfall must be avoided. If the investigator decides to be guided by the appearance of the blood film taken from the baby's circulation, and waits until such time as the textbook description of erythroblastosis is seen, in many cases he will either wait until fatal, or at any rate grievous damage has been done. Treatment must be undertaken early and confidently even where the blood film approximates to normality. It should be remembered that a certain number of normoblasts and reticulocytes will be found in the normal newborn infant's blood. Of far greater significance is the finding of jaundice coupled with any degree of anaemia—the colour index, by virtue of the fact that the red blood count is proportionately lower than the haemoglobin, being consistently high. I think some importance should be attached to the colour index as an indication of the activity of the haemolysis which is going on.

Lack of space precludes explanation of the physiological reasons for this, or description of the technique which may be necessary to obtain haemoglobin-values in the presence of jaundiced serum.

The fact remains that as a simple laboratory estimation of the severity of the disease it is of assistance. The colour index has been above 2 in one of our cases and approaching 2 in several others. As the haemolytic process exhausts itself the value falls. The infant at the same time becomes increasingly anaemic, so that a low colour index does not mean that treatment is not needed. Allowance must also be made for the effect that transfusion will have on the colour index, once treatment has been commenced.

In all cases a sample of blood from the infant should be taken for Coombs' testing, before transfusion. It is important to obtain the specimen before fresh blood is given, because the donated blood may later mask the true state of the blood of the infant (Cathie, 1946), most of which may have been haemolyzed at the time of sampling. This would make the investigation of the baby's blood difficult or impossible. A recent case at the Jessop Hospital for Women, although known to be in an Rh positive baby, by virtue of the antibodies the mother had manufactured, after two transfusions became Rh negative to all tests. One must postulate that all its own blood had been destroyed and it was, in fact thriving on donated blood. In this case the true blood group was determined from the infant's bone marrow, which is not affected by transfusion (Cathie, 1946). We are still waiting to find out when the blood stream again returns to normal. This is not entirely an academic point and has a practical application. At the beginning of this paper, I lodged a plea for more routine antenatal tests in known cases, so that antibody titres can be obtained and studied. Sometimes there are 2 different antibodies present, the titre of each varying, and not necessarily bearing any relation to that of the other. In the infant it is possible to detect the two antigens responsible for these two antibodies. During the course of treatment it

Pregnancy after the Menopause
(A case-report and a review of the literature)

BY

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" Now Abraham and Sarah were old . . . and it had ceased to be with Sarah after the manner of women."

" For Sarah conceived and bare Abraham a son in his old age."

(Gen. xviii, 11 and xxi, 2.)

" And they had no child because that Elisabeth was barren and they both were now well stricken in years " . . . " and after those days his wife Elisabeth conceived . . . (her) full time came that she should be delivered and she brought forth a son."

(Luke, i, 7, 24 and 57.)

THAT Sarah was beyond the menopause when she conceived seems to be indisputable. Her age is alleged to have been 90, but Biblical estimates of age are perhaps more symbolic than factual. There is no indication in the story of Elisabeth as to the incidence of the menopause. The historians of the Bible refer on many occasions to pregnancies occurring at the extreme age: such occurrences were looked upon as miracles and the offspring usually were remarkable in their subsequent careers. It may be that only when the offspring showed supernormal tendencies was the fact that the mother was old considered worthy of comment. It is of course likely that the birth of a mongol would not be recorded, though it is interesting to speculate on the possibility that a mentally defective child born of abnormally aged parents might show in later life the qualities of frenzy or delusion in such a manner as to fit him for the *rôle* of prophet.

Within more recent years documented references to truly post-menopausal pregnancy are rare. There are a number of recorded cases of pregnancy occurring after surgical castration, but of the 11 which have been traced only 5 can be considered valid. In several menses had returned or had continued after the operation, and it must be assumed in every case that some ovarian tissue, normally placed or ectopic, had remained.

Pregnancy after attempted X-ray or radium castration is also reported: in some cases the castration was admittedly ineffective in that menses continued or returned, and in others it must be assumed that the more mature follicles sustained little damage. It is the possibility of such an occurrence, in which the child born may have damaged germ plasm and be sterile, or produce monsters in later life, which causes some workers to be chary of administering X-ray castration to a woman whose reproductive life is still incomplete.

The natural menopause appears to be less fraught with the risk of belated pregnancy. In all, only 15 cases have been traced in the literature, and in several of these the duration of amenorrhoea prior to

delivery was less than 2 years. A distinction must clearly be drawn between cessation of menses and the incidence of the climacteric. Oligomenorrhoea with a flow only once or twice a year, even amenorrhoea of 2 or more years duration, is not uncommonly noted in younger women. In 1 of our own sterility cases there was a history of menarche at 17 years, and subsequent menses at 20 and 25 years, with the association of headaches and flushes suggesting depressed ovarian function. A course of follicle-stimulating hormone was given 9 months after the last recorded menstrual flow and 2 monthly periods occurred, followed by a pregnancy which went to term without incident and was succeeded by regular menses.

Priou (1865) describes a woman aged 72 who had an abortion, and Boldt (1914) had a case of abortion, proved histologically, 1 year after the last menstrual period and 3 years after the onset of menopausal symptoms. Renaudin reports a pregnancy 12 years after the cessation of menses, and Kennedy (1882) had a most astounding patient who is said to have had 5 labours and 1 abortion after her fiftieth year. The duration of amenorrhoea prior to this fertile period of life is not known.

Deliveries of living infants are described by Depasse (1891) 9 years after the menopause, by Buckle (1910) 11 years after, by Underhill (1879) and Levasseur (1873) 2 years after, and by Hann (1902) 3 years after, and the latter quotes a case from Pearson whose period of amenorrhoea was 18 months. Most of the infants appear to have been normal, though that described by Brandt (1922) was an achondroplasic. Ballon (1941) reports a twin pregnancy after the menopause. Mongolism or other mental defect is not recorded in any of these children, but there appears to have been no close follow-up of the cases.

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Additional case-reports come from Mayer (1908), Hirschberg (1910), Hofstätter (1922) and Nurnberger (1924) but the details are not available.

In none of the reported cases is there any mention of return of menses prior to conception, and it must be assumed that in each one the pregnancy followed an ovulation which had not been associated with any menstrual cycle. In the cases of Hann and Buckle menses returned for a short period after the birth, in the remainder there is no mention of subsequent menstrual function.

It is a well-established fact that some ovarian activity may continue long after the apparent menopause, even though there has been a period of flushes and headaches and other subjective symptoms. It is probable that follicular development may continue and ovulation occur at irregular intervals after a symptomatic menopause, and at laparotomy one not infrequently encounters very active looking ovaries even in old women. Nor is it especially rare to find normal external genitalia with healthy vaginal mucosa and a fair growth of Doderlein's bacilli and of glycogen-containing squames many years after the last menstrual period, which findings are strongly suggestive of continued oestrogenic activity. Resumption of menstrual activity years after the menopause has been described, and though in most cases the bleeding is "pseudo-menstrual" and associated with granulosa-cell tumour, or even carcinoma of the uterus, every surgeon must have encountered cases where no such pathology was found to account for the return of uterine bleeding, and where curettings have merely shown a normal proliferative phase.

In the case of post-menopausal pregnancy described below, it was not possible at that time to carry out hormone investiga-

tions. No previous accurate medical observations of the patient were available, but the history was typical of the menopause, and the woman had every right to assume that her days of child-bearing were over.

CASE HISTORY.

Mrs. C. T., aged 45 years, was referred to the Newcastle General Hospital on January 7th, 1944. She gave a history that her last menstrual period had been 3 years previously, preceeded by a period of scanty and less regular losses, and that she assumed that she had passed through " the change of life." The onset of menses had been at 15½ years of age. In spite of her amenorrhoea there had not, however, been any significant flushes or other menopausal symptoms. She had recently contracted scarlet fever and had been in the local isolation hospital, and during her stay there had noticed swelling of her abdomen. This had increased following her discharge from hospital after a stay of 5 weeks, and her doctor had found an abdominal tumour, apparently a pregnancy.

She was a rather stout but healthy-looking woman, grey haired and " motherly " in appearance, who looked all of her 45 years. Physical examination revealed no disease, her blood-pressure was 120/70 and there was an undoubted pregnancy of approximately 30 weeks in size, with a breech presentation. Her obstetric history included 5 previous pregnancies and was satisfactory except for the birth of premature twins, both of which had died.

She attended the antenatal clinic regularly and at 36 weeks the presentation was still a breech. External version without anaesthetic failed, and in view of her previous normal labours and the fact that her pelvis was very roomy, no attempt was made to correct the presentation under anaesthetic.

Labour commenced spontaneously on March 23rd, and the first stage was rather prolonged, though without distress. Delivery of the frank breech was assisted with forceps applied to the after-coming head, and the placenta was expelled 10 minutes later.

Her puerperium was uneventful, but lactation failed completely. She was discharged on the 14th day, and when seen at postnatal clinic 2 months later the findings were those to be expected at a postnatal examination of a multipara. There had not been any further menstrual losses and to date there is no record of return of menses or of another pregnancy. The child weighed 8 pounds 4 ounces at birth and was 21 inches in length, and appeared to be perfectly normal in every way.

It had been expected that hypertension might develop during pregnancy, but the highest recorded blood-pressure was 144/88 with no oedema. Labour was more characteristic of a primipara than a multipara, but this might be explained by the presence of a breech presentation. The only point of special interest is the complete absence of lactation, though breast feeding had been normal in all previous pregnancies.

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The Aetiology of Congenital Torticollis and Certain Associated Deformities, with a Suggestion for Prophylaxis

BY

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No really satisfactory theory of the aetiology of congenital torticollis has hitherto been forthcoming. The main theories have been as follows:

(a) That the condition is due to some central neural defect Osler, 1912). No such defects, however, have ever been demonstrated in support of this theory.

(b) That the condition is an hereditary deformity (Krogius, 1924). This is no longer accepted.

(c) That the condition is due to intrauterine infection (Kader, 1896). Proved cases of intrauterine infection are not accompanied by congenital torticollis. Histological studies, do not support an infective theory.

· (d) That there is prolonged obstruction to the venous return from the sternomastoid and neighbouring muscles during parturition. This results in venous infarction and the formation of the " sternomastoid tumour " (Middleton, 1930). The important work of Middleton and Brooke has received general acceptance, but the exact cause of the venous obstruction needs further elucidation. A "sternomastoid tumour " is not seen in all cases of congenital torticollis.

(e) This theory of venous infarction superseded an older view that the condition was due to arterial occlusion and ischaemia during delivery (Nové-Josserand and Viannay, 1906).

(f) That a uterine malposition is the real cause of congenital torticollis. This theory has had recent support from Chandler and Altenberg (1944), but without any explanation of what the malposition might be.

It is thus left to the obstetricians to confirm or refute this latter theory, and if confirmed to indicate what steps might be taken to prevent the occurrence of congenital torticollis.

With this end in view the antenatal and postnatal conditions of a number of babies born at Mercara Civil Hospital and elsewhere were correlated and viewed in the light of the literature on the subject.

In 53 cases, in all of which the head had been deeply fixed in the brim of the pelvis between 2 and 4 weeks before delivery, the ear which had been posterior showed slight deformity when compared with the anterior ear. Thus, in 28 cases where the back had been toward the right, the right ear was found to be affected. In 25 cases where the back had been towards the left, the left ear was affected. There were also 24 cases seen during the same period where the head had been deeply engaged for a period of 2 to 4 weeks, yet no difference between the 2 ears could be seen.

Thus there was a definite relation between these changes in the ear, when present, and the intra-uterine position of the foetus.

The deformities consisted of:

(a) Thinness and flabbiness of the auricle due to poorly developed cartilage, 43 cases.

(*b*) Flattening of the ear, especially of the helix, 53 cases.

(*c*) The softened helix had turned downwards as if by its own weight in 6 cases.

(*d*) The ear was either flatter against the head when compared with its fellow, or else protruded more. The latter was seen in 15 cases and seemed more prone to occur where the cartilage was especially thin. The former was seen in 48 cases. The protrusion or flattening of the ear was best seen when viewed from the back.

In addition 18 of these babies showed noticeable flattening of the supra-orbital ridge and adjacent part of the forehead on the side opposite to the deformed ear. This flattening of the supra-orbital ridge was best seen when viewed vertically from above.

Since in all these cases the head had been engaged in the pelvis some weeks before delivery it is necessary to consider the exact relationship of the foetal head to the pelvis when deeply engaged. Zweifel's frozen section (1893) of a woman who died at term showed quite clearly that the posterior ear was in relation to the promontory of the sacrum. Thus it seems clear that the minor alterations in the shape of the posterior ear seen in the cases described above were due to continuous pressure on the posterior ear by the promontory of the sacrum.

If one imagines the foetus in Zweifel's section to have engaged rather more deeply, the anterior supra-orbital ridge and adjacent forehead would have been in contact with the antero-lateral wall of the pelvis. This would no doubt explain the flattening of the forehead on the side opposite the affected ear in 18 cases.

It might be argued that such trifling differences between the 2 sides of a baby's face are of no consequence and that a large number of people have slight irregularities in their facial appearance. With this one would agree, except that these trifling changes are often associated with more severe deformities and point the way to an understanding of the aetiology and possible prevention of these.

The following 2 cases demonstrate the close relationship between the frequently occurring slight deformities of the ear on the one hand and the less common but more serious congenital torticollis on the other. If one accepts the view explained above that the pressure of the promontory of the sacrum frequently causes minor ear deformities, then it must also be accepted that if the head is still more deeply engaged there will be changes not only in the auricle but also in the adjacent area of the neck, that is, in the region of the sternomastoid muscle.

A primiparous European, aged 22, had a normal pregnancy and confinement. It was noticed that the head became unusually deeply engaged in the pelvis 4 weeks before delivery. The occiput, which was to the right, could not be felt and the sinciput could only just be felt, in spite of the fact that the patient was a thin woman who relaxed well. Labour, when it occurred, was easy and rapid. The child, a female, was not thought to have any gross abnormality, though a specially detailed examination was not made.

The mother, who was an intelligent woman, noticed soon after birth that the child's right ear was not as well formed as the left. It had a flattened appearance, was thin and flabby and protruded from the side of the head. She also noticed that the child seemed uncomfortable when lying on the left. When the child was a month old the mother realized that this was due to the fact that the child's head " was bent towards the right " which seemed to make it uncomfortable when lying on the left. Medical aid was then sought.

On examination the right side of the neck was seen to be more wrinkled than the left. The sternomastoid muscle was contracted and stood out prominently when put on the stretch. There was no " sternomastoid tumour ". The head could be forced to the left only with difficulty.

The appearance of the ear was as described above. Its cartilage was markedly thinner than that of the other ear. The right cheek was flattened. The left side of the forehead and the left supra-orbital ridge were also definitely flattened.

The condition of the neck responded to conservative treatment of forcing the head over to the left twice a day. A cloth skull cap with ear pieces was worn at night to keep the protruding ear in position.

The asymmetry of the child's face could still be seen when it was 8 years old.

Two years later the mother gave birth to a male child. On this occasion the head again entered the pelvis some 8 weeks before the expected date of delivery, in the right occipito-anterior position. An accidental type of antepartum haemorrhage occurred however, and a child weighing 4½ pounds was born 4 weeks before the expected date of delivery. On careful examination of the baby's head and face, very slight inequalities between the 2 sides, similar to those seen in his sister could be made out. The sternomastoid muscles were normal. By the time the child was a few months old no trace of the facial asymmetry remained.

It is tempting to think that this baby, too, might have suffered from congenital torticollis but for the premature delivery.

A similar, though less striking case, was that of a Mohammedan woman who, 3 weeks after the birth of her first child, a male, brought it to hospital to have its septic umbilicus dressed. She had been delivered at home by a female doctor who, on questioning later, stated that the head had been unusually deeply engaged in the pelvic inlet some weeks before labour, and that the foetus had been in the left occipito-anterior position.

While the umbilicus was being dressed it was noticed, for the first time, that there was a mild degree of left-sided torticollis. The left side of the neck was more wrinkled than the right and the left sternomastoid stood out prominently when the head was straightened, which could be done only with difficulty, causing obvious pain. On further examination the left ear was found to be thinner and flatter than its fellow. The left maxilla and right supra-orbital region were flatter than on the opposite side.

With appropriate treatment the torticollis disappeared but after 6 months the facial and auricular inequalities were still recognizable.

One case of congenital torticollis was encountered which showed that on occasion the ear changes may be very severe.

A Hindu male, aged 26, applied for work at the hospital. It was seen that he was suffering from a moderate degree of right-sided torticollis, and severe deformity of the right side of his face and ear. He stated that he had been born with these deformities. He was the eldest child. None of his brothers or sisters had any abnormal appearance.

On examination the right sternomastoid was fibrosed and contracted. It stood out prominently when put on the stretch. The upper 1½ inches was much indurated. His face showed the usual stigmata associated with congenital torticollis, being comparatively undeveloped on the affected side. The distance between the outer angle of his right eye and the right angle of his mouth was only 2 inches whereas a similar measurement on the left side was 2¾ inches. The chin pointed to the sound side slightly. The mastoid process and maxillary process were both flattened on the affected side. There was, however, no difference between the 2 sides of his forehead.

The most striking feature of the case was the right auricle, which was represented by only a small fleshy lobule half-an-inch in length. There was no external meatus but on X-ray examination the bony meatus was seen to be present. A loudly ticking watch could be heard half an inch from the affected ear. Pressure over the bony meatus caused sharp pain.

It is interesting to note that though descriptions of congenital torticollis give adequate attention to the flattening of the face and forehead no mention seems to have been made of auricular deformities, although in the photographs accompanying such descriptions inequalities in the ears can sometimes be seen (Rose and Carless, 1927).

Out of Chandler and Altenberg's 101 cases of congenital torticollis, 3 had Erb's paralysis. Middleton likewise found congenital torticollis to be a not infrequent

accompaniment of this condition. These authors attribute the paralysis to traumatic delivery. Although trauma may be the cause in some cases it is far more likely that the same factors which caused the torticollis caused the Erb's paralysis too, that is, that the pressure of the sacral promontory catching the neck a little lower, was sufficiently prolonged to cause permanent damage to the upper trunk of the brachial plexus. Chandler and Altenberg had one case with a congenital short arm associated with congenital torticollis. Here the pressure must have been sufficient to interfere with the nutrition of the whole limb-bud, leaving it permanently shorter.

DISCUSSION.

On the basis of the above considerations one can state fairly confidently that congenital torticollis, as well as certain associated conditions, is due to the continuous pressure on the parts when the head engages in the pelvis unusually early and deeply.

The "sternomastoid tumour" which sometimes develops 10 to 14 days after birth in association with congenital torticollis, is undoubtedly a secondary phenomenon and not the primary lesion as was once thought. Chandler and Altenberg consider it to be a fibroma forming in a muscle, previously damaged by intrauterine malposition, being traumatized during delivery.

Congenital torticollis is never bilateral. It occurs on the right side in 56.4 per cent of cases according to Eddy (1932) or 55.4 per cent according to Chandler. Since the back is usually on the left this right-sided preponderance requires some explanation. Presumably the well-known tendency for the occiput to be directed somewhat posteriorly when it is to the right, makes the sternomastoid muscle more likely to come directly in contact with the sacral promontory.

The head normally becomes fixed some weeks before term in a primipara. Thus a higher proportion of cases of torticollis amongst first babies is to be expected. Middleton found 43 of his 64 cases amongst first babies.

At first sight the comparatively large proportion of children with congenital torticollis who have been born by breech presentation might appear to be inconsistent with the views expressed above. How could such cases have been caused by pressure of the sacral promontory on the child's neck ? Chandler and Altenberg, who found 30 cases of breech presentation amongst their 101 cases of congenital torticollis, suggest that intrauterine torticollis prevents engagement of the foetal head. It is well known that the foetus changes its position frequently, and having once developed torticollis in the manner described above, should the head then disengage, the torticollis might well militate against re-engagement of the head, thus favouring the assumption of the breech position.

The possibility of preventing congenital torticollis and associated conditions.

Where the head is found unusually deeply engaged in the pelvis during the 36th week or earlier and remains in this position, it might well be that induction of labour some weeks early might prove beneficial. Further work will be required before any definite indications for induction of labour for this condition could be given.

In any case after delivery in such circumstances a careful inspection of the baby is necessary to exclude torticollis, Erb's paralysis, etc. Congenital torticollis is easily missed during the first months of life,

while the earlier treatment is commenced he better.

CONCLUSION.

The close relationship between certain congenital abnormalities of the ear, congenital torticollis and some cases of Erb's paralysis is demonstrated.

From a study of a series of patients and the literature on the subject it is concluded that these conditions are due to the foetal head and neck entering the pelvis earlier and more deeply than usual before labour, where, having lost the protective cushion of the amniotic fluid, the parts are subjected to continuous pressure chiefly by the promontory of the sacrum.

Prophylaxis by induction of premature labour is a possibility.

In all cases where the foetal head has been unusually early and deeply engaged, the baby's head and neck should be very carefully inspected at birth to make sure that mild cases of torticollis or Erb's paralysis are detected.

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The Treatment of Intractable Cases of Essential Pruritus Vulvae

BY

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THE problem of the pathogenesis and therapy of pruritus vulvae cannot be regarded as yet solved. This fact explains the innumerable methods of therapy. In most cases pruritus vulvae does not imply a serious disease. Its severe forms, however, cause great suffering to the victims to such an extent that their social intercourse and especially their rest is disturbed.

The essential symptom is an itching and burning feeling in the vulva and its vicinity, and in many cases in the region of the anus as well, and may be intermittent or continuous.

According to the classification generally used in the literature there are 2 separate forms of the disease: (1) the symptomatic (exogenous) pruritus which appears as an accompanying symptom of other diseases; (2) the essential (primary) form which represents a true disease entity.

The pathogenic factors and therapy of symptomatic pruritus vulvae are generally known. The problem is presented by the essential (primary, endogenous) form as there are cases of this disease which do not respond to any local or general treatment whatever. These cases are a real " crux medicorum " causing great suffering to the patients and presenting a big problem for the medical attendant.

In a number of cases the pathogenic factor cannot be identified even by the most thorough investigation, and difficulties are increased by the fact that a combination of factors is present in some cases. In these only symptomatic treatment can be applied and if this is protracted a vicious circle is created, itching followed by scratching and energetic scratching increases itching.

The *method described below would* appear to be original as there is no data in accessible literature as to its previous use. It has some resemblance to Ball's procedure (1905) which, in cases of pruritus ani, makes semicircular incisions on both sides of the anus and undermines the edges of the wounds. Caroll W. Allen (1920) makes radial incisions around the anus and puts iodoform gauze under the " skin-ribands," removing it after a week, thus preventing the skin from adhering to its base.

Before describing the procedure I want to emphasize that it is essential to exclude the existence of local pathogenic factors by the most thorough investigation before surgical intervention, and also to make the point that proper application of the procedure described below is restricted to cases of essential pruritus and is not advisable in cases of kraurosis vulvae.

The operation is performed as follows. After thorough identification of the itching area the whole diseased skin-surface is infiltrated subcutaneously with 0.5 per cent novocaine-adrenalin solution. Thereafter a number of 2 cm. long transverse incisions are made. It is advisable to make the incisions in a certain succession. The

FIG. 1

FIG. 2.

FIG. 3.

FIG. 4.

A H

procedure described below shows the method used in cases in which pruritus affects the mons veneris, the vulva and the anal region as well.

Through the incisions, by means of scissors with thin, slightly bent blades, frequent cuts are made subcutaneously in order to separate the skin from the underlying tissue which is within reach. The first incision is made 2 cm. above the tip of the coccyx (Fig. 1). From this incision the skin of the posterior perineum can be separated up to the mucous membrane of the rectum. An incision is made medial to the ischial tuberosity on each side (Fig. 2). From these incisions the upper part of the anal region, the perineum and the lower parts of the labia majora and minora can be reached. Incisions are made on each side of the labia majora (Fig. 3). From here the rest of the labia majora and minora and the region of the clitoris are accessible. The mons can be reached by long-handled scissors from these incisions. If need be an incision may be made above the clitoris in order to separate the skin of the mons and around the clitoris. The number of incisions depends on the extent of the itching area.

After finishing separation of the skin each incision is immediately sutured (Fig. 4). The subcutaneously injected novocaine-adrenalin solution temporarily prevents bleeding; minor or major subcutaneous haemorrhages, however, cannot be avoided as a consequence of the operation. Serious haemorrhages, however, have not been experienced. These subcutaneous haemorrhages actually increase the effect of the operation by separating the skin from its base during the time of absorption. Great importance is attached to postoperative treatment of the separated skin. The greatest need is to keep the skin dry by frequent sprinkling with neutral powder. No bandage is applied. Owing to abolition of scratching the excoriations heal in a very short time. On the first days after the operation a slightly painful and burning feeling usually develops and for that administration of an anodyne is necessary.

The first operation was performed in August 1945, and since then 8 patients have been operated on in this way: in 7 cases as separate operations and in 1 case (kraurosis vulvae) as a supplementary operation to vulvectomy. In this case itching extended around the anus and after vulvectomy the skin of the anal region was, therefore, also separated from its base.

Prior to the above operation these cases were treated unsuccessfully by numerous methods. Two years was the shortest time during which the patients suffered from pruritus vulvae. In one case the pruritus was treated for 20 years without improvement. After operation the pruritus promptly ceased and the patient has not complained since.

All the patients have been similarly treated and the complaints were of the same nature, thus it is sufficient to give the record of only one case. She was the first to be operated on by this method.

Case Record.

Mrs. T. M., aged 51; Menarche 16. Since then menstruation every 21st day, lasting for 4 to 5 days. No cramp, last period in 1939. She had had 1 normal delivery and 2 spontaneous abortions.

Two years ago pruritus began on the vulva. Since then constant itching, increased chiefly at night. Prior to admission she was given folliculin (70 mg.) and received X-ray irradiation. No improvement was obtained. She was suffering from intolerable nervousness.

Condition on admission. Emaciated patient; no palpable abnormality in the abdomen. Urine normal. Red-blood cells, 4,300,000. White-blood cells, 7,000. Sedimentation of red-blood cells, 16 mm. in 1 hour. Dellamartina-Mester reaction showed no deficiency of vitamins. Gynaecological examination showed no abnormalities except

synchronously. On separation of the heads the inner carotid pulsations were difficult to observe and palpate. The faces were identical, both blinked normally and separately. The right head was facetted in the temporal area by the left one which was slightly larger in all diameters. The fontanelles and sutures were normal for the stage of maturity. The heads shared the body evenly on the wide shoulders. Posteriorly, at the acromial level, there was a fixed protrusion bearing a marked resemblance to the hump of a well-known humorous literary character (Plate IV). The monster passed some urine through a normal penis. Nothing abnormal was noted in the rather massive arms and smallish legs. It survived about 20 minutes and apparently died physiologically altogether.

Its birth weight was 7¼ pounds. The combined bi-parietal diameter was 19 cm., and the bisacromial 17 cm.

After delivery, further radiological examinations were made of the foetus. This confirmed the skeletal appearances demonstrated on the films taken before delivery.

The upper 7 ribs, between the 2 vertebral columns, were seen to bow upwards and were fused together in the midline, with a rudimentary scapula at the extreme upper end.

To study, grossly, the vascular system, Diodine solution was injected into the right foetal common iliac artery (Plate V). At first 6 ml. were injected. This ran up this vessel into a vessel running alongside the right vertebral column. This latter vessel joined on to the lower part of the left-sided aorta at L.4 level.

There was only 1 heart lying in the thorax almost centrally between the 2 foetuses. From this the aortic arch rose into the left foetus and descended normally to the lumbar region. From the arch arose an innominate and left common carotid artery. At the lower end of the left aorta

a left common iliac artery was seen. The right aorta arose from the left one at L.4 level and ran up alongside the right vertebral column, presumably supplying the right head and neck.

After 20 ml. had been injected a single superior and inferior vena cava were seen.

To study the gastro-intestinal system a catheter was passed down each oesophagus and thin barium was injected down each catheter (Plate VI).

The right oesophagus appeared to end blindly at D.2 level, the catheter doubling back at this level and no barium passing lower down. The left-sided oesophagus passed into a normal-looking stomach situated normally in the left side of the abdomen. Some of the barium passed into the upper small intestine, which was lying on the right side of the two foetuses. Presumably, therefore, there was a common gastro-intestinal system below the diaphragm for the two foetuses.

Since 1900, 47 cases of dicephalic monsters have been reported. So far as can be traced 2 of these were radiologically diagnosed antenatally (Hunter, 1941; Brailsford, 1942). In the second of these an almost identical foetus but with 2 central rudimentary arms is illustrated. It is not stated whether this fusion was discovered antenatally but presumably it was, since Brailsford (1944; 1942) draws attention to the great importance to the obstetrician of recognizing such a fusion before birth. He also draws attention to the antenatal signs suggesting fusion, e.g. heads bearing similar relation to the trunks, spines parallel to each other and abnormal interskeletal ribs. Such signs are clearly seen in the present case. One only of these cases (Brailsford, 1944) was delivered by Caesarean section, having been clinically diagnosed as probable twins, the indication for the abdominal method of delivery being an antepartum haemorrhage at the 36th

PLATE I.
Postero-anterior View.

N. & O.-J.

PLATE 11.
Tilted View to Show Foetal Pelvis.

N. & O.-J.

PLATE III.
Anterior View.

PLATE IV.
Posterior View.

PLATE V.
Arterial System after 20 ml. Diodine.

N. & O.-J.

PLATE VI.
Barium in Oesophagus and Stomach.

week. In the present case it would have been possible to deliver vaginally in spite of the wide shoulders. Stander (1945) refers to the fact that the first head and then the second head can be extracted if a breech. The free lateral movement of the heads in this case might have allowed this if the 2 aftercoming heads did not try to engage together. The decision to deliver abdominally, however, has left us with a patient with an undamaged birth passage and she has been advised that, in view of the great rarity of the condition, there is no contra-indication to further pregnancy.

After the various postmortem investigations referred to were carried out, it was appropriately sent to the Bland Sutton museum at the Middlesex Hospital.

We are especially indebted to Dr. A. M. Thomas, who took the photographs, to the Librarian of the British Medical Association, and to the anaesthetist and residents at the Wrexham Hospitals.

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Haemorrhagic Disease of the Unborn

BY

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HAEMORRHAGIC disease of the newborn is a well-known entity, characterized by bleeding, chiefly from the bowel, due to prothrombin deficiency at birth.

Bleeding is usually first noticed from the bowel, from the first to the fourth day of life, and is shown by the presence of bright blood or by a tarry stool containing altered blood. This first tarry stool is sometimes mistaken for ordinary meconium, as it occurs usually about the time when the character of the stool is changing from meconium to normal yellow.

Bleeding can occur from any of the mucus surfaces, or under the skin, and sometimes the onset is so severe that the infant dies before any treatment can be given.

The peculiar interest of the case described here is that the disease was discovered before birth.

The details are as follows:

A primigravida, aged 34, had been married for 10 years. She attended the antenatal clinic regularly, and to her delight was found to have a twin pregnancy.

At the 36th week she developed signs of toxaemia with a sudden rise of blood-pressure to 170/100 and with oedema of the legs. She was brought into hospital for rest and her blood-pressure dropped to 128/80.

X-rays showed the first twin to be presenting by the breech and the second by the vertex.

Labour commenced spontaneously at the 37th week at 10 a.m. on March 12th, 1947.

Four hours later the patient was reported to be passing meconium in the vaginal discharges. On examination it was seen that this meconium was a typical tarry stool of haemorrhagic disease of the newborn, and that it also contained a little bright blood. A portion was sent to the laboratory for confirmation. At this stage the pains were strong, the os was only slightly dilated, and the breech was above the brim.

The mother was given omnopon, gr. 1/3; scopolamine gr. 1/150; and Prokayvit (vitamin K) 20 mg.

After 1½ hours, at 3.30 p.m., there was the passage of still more blood from the infant, and the foetal heart dropped to 80. There was no other cause found for foetal distress. About 120 ml. of the tarry material had been passed by this time.

It was considered that if labour were to continue normally the first child would die from haemorrhage before it could be delivered, but that immediate Caesarean section, followed by blood transfusion might save the infant.

The position was explained to the mother, who at once agreed to any measure that would give a chance of the child being saved.

At 4 p.m. a lower segment Caesarean section was performed under cyclopropane anaesthesia. The first twin was very limp at birth, and was given an immediate transfusion of 40 ml. blood with 10 mgm. of Synkayvit (vitamin K) into the cord. The second child was healthy. These were binovular twins, the first being female and

the second male, with birth-weights of 4 pounds 9 ounces and 5 pounds 5 ounces. Some tarry meconium was still present around the anus of the affected child at birth and rectal examination confirmed the presence of blood in the rectum.

The infant was given 10 mgm. of Synkayvit daily.

On the fourth day there was a second small tarry stool, but, after this, no further bleeding. The birth-weight was regained by the thirteenth day, and the mother and both infants were discharged on the twentieth day. The mother made an uninterrupted recovery.

The interesting features of this case are the occurrence of bleeding before birth, in one only of binovular twins, with recovery after delivery by Caesarean section followed by blood transfusion.

A similar case, with less fortunate ending, is also described below:

Mrs. D., aged 26, was a primigravida who was healthy and who had an uneventful pregnancy. She came into labour at term, and labour progressed normally. At full dilatation, after a first stage of 6 hours, the foetal heart was regular and clear. The membranes did not rupture but presented at the vulva and were ruptured artificially. Just before rupture, the foetal heart was 120, but 10 minutes afterwards the heart sounds disappeared completely. The infant was born by natural forces 10 minutes after the heart sounds ceased. There was a gush of bright red blood as the head was born. At birth the infant was apparently dead. It was absolutely white, and bright red blood was pouring from its mouth and nose. As the blood was cleared with a mucous catheter more blood appeared. It was unlikely to have been inhaled, because the infant had never breathed.

Lobeline and coramine were injected into the cord and respiration commenced after about 5 minutes. The heart was beating very faintly. The child was limp and toneless, and made no effort to move or cry. A little fresh bright blood still appeared through its nose, and it was agreed that it was suffering from haemorrhagic disease of the newborn—a massive haemorrhage having probably occurred just before birth, after which the foetal heart had ceased.

A blood transfusion was given about half-an-hour after birth. Group O Rhesus negative blood 5 ml. were given into the cord. No more blood would run into the cord, therefore a further 10 ml. were given into an arm vein and 10 ml. were also given intramuscularly into each buttock.

The child's condition improved considerably. A faint pink tinge of the skin appeared, the conjunctivae became deeper pink—having previously been colourless—and muscle tone improved sufficiently for the infant to resist the intramuscular injections. Breathing was still shallow, and the heart was feeble. The child was left in its cot to rest and recover, but during the night it had another small haemorrhage and died.

Postmortem examination showed considerable fresh bleeding in the duodenum and upper part of the jejunum. There was no evidence of ulceration.

Obituary

CHARLES PHILIP BRENTNALL
M.C., M.B., Ch.B., F.R.C.O.G.

C. P. BRENTNALL died in Manchester on June 26th, at the age of 56. Son of the Rev. Edward Brentnall, M.A., he received his early education at St. Paul's School, London, and the Manchester Grammar School and then, having gained the Dreschfeld Scholarship, proceeded to Manchester University to study Medicine. Whilst in his second year his father moved to a living in West Lancashire, so Brentnall transferred to Liverpool University. There he had an unusually brilliant career, gaining Distinction in the M.B. Examinations in Anatomy, Pharmacology and Pathology, and also winning the Gee Prize.

He qualified in 1915 and after holding the post of House Surgeon to the Liverpool Northern Hospital joined the Royal Army Medical Corps. He served in the field in Gallipoli, Palestine and France, rose to the rank of Major and was awarded the Military Cross. After the war he returned for a time to work in Liverpool and was then appointed resident to the Hospital which he served for the rest of his life, St. Mary's, Manchester. At St. Mary's he was successively House Surgeon, Resident Obstetric Officer, Resident Surgical Officer and Registrar, and was elected to the Honorary Staff in 1925.

Brentnall's work as a gynaecologist was typical of the man. His approach was gentle. In consequence his surgical results were outstandingly good and his technique served as a model for his juniors. As was to be expected, he built up a large consulting practice and his services were in demand over a wide area. His appointments outside Manchester included those of Honorary Obstetrician to the Stretford Memorial Hospital and Honorary Consulting Gynaecologist to the Warrington Infirmary.

A Foundation Member of the Royal College of Obstetricians and Gynaecologists, he served on the Council for 6 years, being raised to the Fellowship in 1938. He was also a member of the Gynaecological Club.

Brentnall's contributions to gynaecological literature were made largely in the form of communications to the North of England Obstetrical and Gynaecological Society of which he was a Fellow. A regular attender of meetings he could always be counted upon to add something of interest to a debate or to give a word of encouragement to a junior member. It was indeed tragic that shortly after his election as President he should have been stricken by the illness from which he eventually died. During recent years he has published 3 papers in the *Journal of Obstetrics and Gynaecology of the British Empire*: "Local anaesthesia in vaginal operations"; "Arrhenoblastoma of the ovary during pregnancy"; and "A note on Fothergill's Colporrhaphy."

In his private life Brentnall was singularly fortunate and he was never so happy as when, in his own home he could enjoy the companionship of his family and friends. He leaves a widow, a daughter, and a son who is studying medicine.
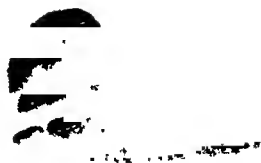
CHARLES PHILIP BRENTNALL

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At the meeting of the Council held on May 31st with the President, Mr. W. Gilliatt, in the Chair, it was announced that Field Marshal the Rt. Hon. Jan Smuts, P.C., had accepted an invitation to become an Honorary Fellow.

To mark the grant of the Royal Charter of Incorporation by H.M. the King on March 21st the four surviving signatories to the Articles of Association, whereby the College was founded, were elected to the Honorary Fellowship:

Professor J. M. Munro Kerr.
Professor C. G. Lowry.
Sir Ewen Maclean.
Sir William Fletcher Shaw.

The following were elected to the Council to replace those retiring in statutory rotation:

As Representatives of the Fellows—

Dugald Baird, Aberdeen.
Alice Bloomfield, London.
Gilbert Innes Strachan, Cardiff.

As Representatives of the Members—

John A. Stallworthy, Oxford.
Arthur M. Sutherland, Glasgow.
Robert James Wotherspoon, Glasgow.

A Standing Committee of the Council to be known as the Australian Regional Council has been set up in Australia. Dr. F. A. Maguire, of Sydney, has been appointed Chairman. The Australian Regional Council will act as a representative Committee of the Council of the College in discussions and negotiations affecting the practice of obstetrics and gynaecology in Australia. Professor B. T. Mayes, of Sydney, will act as Honorary Secretary of the Australian Regional Council.

The following were admitted to the Fellowship of the College:

Malcolm Duncan Black.
James Stoddart Hevell.
Jerusha Jhirad.
Thomas Nicol MacGregor.
Robert Newton.
George Drury Shaw.
Gerald Spence Smyth.
Harry Silvester Waters.
Bryan Williams.

The following were admitted to the Membership of the College:

Duncan Ballantine.
Margaret Rosalin Biggs.
William Stewart Campbell.
John Barr Cochrane.
Sydney Joel Cohen.
Henry Vincent Corbett.
Albert Davis.
John Roscoe Dickinson.
Bessie Dodd.
Morag Dods.
Robert Chalmers Gill.
Jean Lilian Hallum.

Ronald Fox Lawrence.
Thomas Henry Lawton.
John Malcolm McBride.
Reginald Arthur Edward Magee.
Michael Kieran O'Driscoll.
Stewart Sandeman Favell Pooley.
Louis James Quinn.
Robert Burnett Salter.
Philip Cedric Thomas.
Kathleen Mary FitzGerald Worrall.
James Lawrence Wright.

A Meeting of the Council was held in the College House on Saturday, 26th July, 1947, with the President, Mr. W. Gilliatt, in the Chair.

Mr. W. Gilliatt, C.V.O., M.D., M.S., F.R.C.P., F.R.C.S., P.R.C.O.G.; was re-elected President.

The following officers were also re-elected:

Vice-Presidents.
Sir William Fletcher Shaw, M.D., M.M.S.A. (Hon.), F.R.C.O.G.,
James M. Wyatt, F.R.C.S., F.R.C.O.G.

Honorary Treasurer.
Arthur A. Gemmell, M.A., M.D., F.R.C.S.E., F.R.C.O.G.

Honorary Librarian.
F. W. Roques, M.A., M.D., M.Ch, F.R.C.S., F.R.C.O.G.

Honorary Curator to the Museum.
Aleck W. Bourne, M.B., B.Ch., F.R.C.O.G.
H. G. E. Arthure, M.D., F.R.C.S., M.R.C.O.G., was elected Honorary Secretary.

The following Candidates were elected to the Membership of the College:

Segulla Jacob Aptekar.
Henry Bernard Bagshaw.
George Henry Bancroft-Livingston.
Solomon Bender.
Isabella Russell Bishop.
James Tweedie Swan Brown.
Gwendoline Eardley Cockren.
James McDiarmid Corston.
George Archibald Craig.
Kenneth Joseph Robson Cuthbert.
Rudolph Walter Danziger.
Burjor Cavas Dastur.
Josephine Alice Davidson.

Norman Eric Corrigan de la Hunt.
William Powell Greenlie Dickson.
Ian Alexander Donaldson.
Sara Margaret Field-Richards.
Thomas Benedict FitzGerald.
John Browne Fleming.
Ian Tuke Fraser.
Alen Macpherson Giles.
Adam McMurtrie Graham.
Earle Francis Beattie Hamilton.
Lois Edythe Hurter.
David Worsley Jones.
Eileen Iris Jamieson.

Robert John McConnell Jameson.
David Hugh Lees.
Max Lipsits.
George Ian Louisson.
William Love.
Joan Edith Warner Mackie.
Cecil John MacKinlay.
James Theodore Mair.
Parveti Malkani.
Wilfrid George Mills.
Philip Rene Mitchell.
Mary Louise Neville.
Edwin Ronald Ormerod.

Horace Gordon Page.
Stephen Sackville Parlee.
Nancy Perry.
Elliott Elias Philipp.
John Geoffrey Pritchard.
Eric Eli Rawlings.
Elisabeth Margaret Rose.
Dorothy May Satur.
David Arnold Fletcher Shaw.
Denys John Neal Smith.
James Walker.
Ada Sau Wong.

BOOK REVIEWS

"Antenatal and Postnatal Care." By FRANCIS
J. BROWNE. Sixth edition, 1946. Churchill. 644
pages; 90 illustrations. 24s.

To the reviewer's mind this is the most valuable
book of its kind in any language. Its information
is both comprehensive and considered; it is a
"safe" book from the points of view both of
candidates for higher obstetric degrees and for the
general practitioner who must meet the obstetric
emergency from time to time. Both the ideal
and the practicable are preached; in these days
Browne shows that the two can usually be identi-
fied. The ground surveyed is immense; there is
very little of importance in the whole field of
obstetrics that is not admirably discussed.
Special praise must be given to the section on
general diseases of the pregnant woman, and par-
ticularly to the management of cases of diabetes,
thyrotoxicosis and heart disease.

The treatment of abortion is particularly well
considered. Despite recent pronouncements in the
medical press, the reviewer's own extensive ex-
perience of septic abortion suggests that Browne's
advocacy of conservative treatment is still the best
even in this era of the sulphonamides and
penicillin. Professor Browne is a world-acknow-
ledged expert on the toxaemias of pregnancy—the
chapters dealing with the subject are the latest
word and written with unusual grace and lucidity.

Trial of Labour is very well discussed and this
knotty subject very fairly considered from every
angle and opinion. If detraction be permissible,
the reviewer would like to advise that the italicised
" definition " of Trial Labour on page 296 should
be removed. Given such prominence it is bound
to be remembered as authoritative although the
rest of the section shows how rarely this defini-
tion obtains and how fraught with disaster is its
rigid adoption. The reviewer rejoices that Pro-
fessor Browne himself considers premature rupture
of the membranes virtually to cancel the trial.

The chapters on pyelitis are among the best in
the book. The aetiology, diagnosis and course of
the disease are authoritatively discussed; the
reviewer must, however, deplore the recommenda-
tion in this widely read and respected publication
of quite unnecessarily large doses of sulphonamides
for the treatment of the infection. From trial in
the laboratory and in clinical practice both here
and in America it has been shown again and again
that a maximum of 1.5 to 2 g. of the chosen
sulphonamide in 24 hours is all that is necessary.
The kidneys in pregnancy are not in such a state
as to be called upon to excrete massive doses of a
drug which is peculiarly prone to cause renal
damage. We hope to see this considered in future
editions. If these small doses (1 tablet of 0.5 g.
three times a day) fail, either the patient has
vomited the drug, which should then be given
hypodermically, or renal anatomy or pathology
of an obstructive nature exists and should be
remedied.

Sulphathiazole, which Professor Browne recom-
mends as a more strongly bacteriostatic agent in
serious cases should *never* be used in renal infec-
tions as, with sulphapyridine, it has the worst
reputation for the production of crystalluria.

Antenatal and Postnatal Care is written through-
out in a most attractive style which must account,
apart from the great value of the matter, for the
extraordinary affection in which the book and its
author are held throughout the English-speaking
world. Apart from the pleasure the manner of the
book gives to those whose mother tongue is
English, the reviewer has been told again and again
of the ease with which the author's sense can be
grasped by the foreign, and especially the oriental,
student, who usually appreciates the merely did-
actic.

"The Rhesus Factor." By G. FULTON ROBERTS,
M.A., M.B. W. Heinemann, Medical Books,
Ltd., London. 3s. 6d.

THERE is without doubt a great demand for a lucid
summary of knowledge about the Rh Factor.
Unfortunately there are few people who are in a
position to write a comprehensive and authorita-
tive account, for it should include sections on the

theory and genetics of the factor, on its clinical significance, and on the serological tests for its various antigens and antibodies. Developments have been so rapid that only a person actively engaged in research in all these fields is likely to be able to assess correctly the value of each different new contribution and to form from the mass of data a clear and true picture of the whole.

The present book, which is very short, gives a good elementary account of the theory of the subject and of its clinical importance.

One is very pleased to find an exposition of Fisher's CDE nomenclature, but sorry to see it relegated to a subordinate position. Most teachers, both in this country and, apparently, in the United States and elsewhere, are finding that Fisher's scheme is the only one which can be easily expounded. The original symbols introduced by Wiener are very convenient for use in speech but, since they only allot a single sign for a complex of antigens, their relationship to one another is very difficult to explain and harder still to commit to memory. Fisher's scheme, with its use of single letters for single antigens and thus of combinations of letters to describe genes, is cumbersome but far more easily understood.

With regard to the clinical side of the book, the main facts are clearly set out and illustrated by useful case-histories, and the treatment of the infant affected with haemolytic disease is described. With regard to the latter, one feels that the author has perhaps not quite a large enough personal experience to be able to write a really satisfactory account.

One may summarize the book by saying that it is a useful introduction to the subject; but it must be added that a person who has mastered the elements and wishes to obtain authoritative, up-to-date information on any of its manifold aspects must still be given a list of references to recent medical journals. P. L. MOLLISON

"Textbook of Obstetrics." By GILBERT I. STRACHAN, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G., with 3 colour plates and 323 illustrations in the text. London: H. K. Lewis & Co., Ltd. 1947. Price 45s.

THE publication of this new textbook of obstetrics from the Welsh National School of Medicine and dedicated by the author to his friend and colleague Sir Ewen Maclean may well be regarded as an event in British obstetrics. It is not, as so many textbooks are, written by one at the outset of his professional career but by an obstetrician and teacher of ripe experience who has served a long apprenticeship to his specialty, who is rightly regarded by his colleagues as a leader in his profession and who has himself contributed largely to knowledge of its theory and practice. In the words of his preface the book embodies " the experience of many years of teaching and practice in this specialty . . . while the opinions of others have been freely referred to, the personal aspect of the matter has been stressed . . . one thing has been emphasized throughout the book, namely, the importance of conservatism, and the avoidance of unnecessary interference, the policy of hands off." The book, considering the stringency of the times, has been remarkably well turned out by the publishers, the illustrations are numerous, and mostly original, and we have been unable, in spite of careful perusal, to discover more than one or two misprints. To get this less pleasant part of the business over and done with we would point out that the genitive " pubis " is used more than once instead of the nominative " pubes ", that " ventri suspension " should be " ventro suspension " and that, especially in these days of paper shortage, we do not like the expression " full term."

It is a pity that where so many references to literature are given there is no bibliography. Might we suggest that this want should be supplied, preferably at the end of each chapter in the next edition? This is because in our opinion the book will appeal not only to harassed students preparing for final examinations but to a far wider circle of readers including many preparing for higher examinations, and who may therefore wish to consult original papers.

In a book so generally excellent there are few subjects for criticism. It is noteworthy, however, that Professor Strachan still thinks that the normal true conjugate of the pelvic inlet measures 4 inches (10 cm.). This is all the more strange as it is evident from the text that he is well acquainted with the work of Hastings Ince and Matthew Young. These workers made a radiological survey of the pelves of 500 consecutive women in the antenatal clinic at a London hospital. One of their

most important findings was that the mean length of the true conjugate was 4½ inches. In diagnosis of contracted pelvis no mention is made of the importance of measuring the patient's stature, a very simple procedure that takes little time and yet gives useful information. If it is under 5 feet contracted pelvis is often though of course not invariably present. In the description of the measurement of the diagonal conjugate it is advised that the patient should be on her back. If she is on her left side with her knees well drawn up it is possible to press the perineum much farther back and even in a normal pelvis to reach the sacral promontory with the examining finger. The section on placentation is excellent and well illustrated, as would be expected from one who has himself published two standard monographs on the physiology and pathology of the placenta.

The chapter on placenta praevia contains sound teaching. It is good to note that the use of the terms first, second and third degrees of placenta praevia is advised rather than the confusing terms lateral, marginal, etc. The value of expectant treatment is emphasized but no mention is made of the advisability of passing a speculum as soon as possible after admission in order to inspect the cervix and exclude certain extraplacental causes of bleeding, especially cancer of the cervix. The procedure is simple and does not entail any risk of introducing sepsis or causing further haemorrhage. In the treatment of contracted pelvis Professor Strachan advocates trial labour in contradistinction to inducing premature labour. The reasons he gives for this are that, first, unnecessary inductions are often done, and, secondly, that the neonatal death-rate amongst the premature infants obtained by induction is high. One wishes that the foetal and neonatal mortality from trial of labour in Cardiff had been given. We have the impression that in general it is lamentably high and in one large series quoted in the American literature it is 20 per cent in cases where the labour had lasted 30 hours or more. It is doubtful if this can be much reduced except by doing more Caesarean sections either with or without a preliminary test of labour. If induction of premature labour were, like test of labour, only carried out in the best surroundings by those with special experience in the diagnosis and management

of contracted pelvis, and if the diagnosis of contracted pelvis were always confirmed, as it should be, by X-ray pelvimentry, and if inductions were not done till the end of the 37th week we are of opinion that the results from induction might compare favourably with those from trial labour and the Caesarean section rate be considerably lower.

The section on external prophylactic version is excellent and the illustrations of this operation are the best that we have seen. In Cardiff the version is not attempted till 36 weeks which we think is 2 or 3 weeks too late. The importance of obtaining an X-ray picture before attempting it is rightly emphasized but no mention is made of the advisability and indeed the necessity for accurate X-ray pelvimetry if the attempt at version fails and we are faced with a breech delivery, for as is pointed out a breech delivery through a contracted pelvis can be an exceedingly hazardous enterprise. The statement is made that if, in a breech delivery, the cord is not pulsating after the breech is born, the foetus is dead. This is not by any means always so. Neither can we agree with the advice given in the section on fibromyomata in pregnancy that, where Caesarean section is necessary, myomectomy should be done at the same time as the section. The safety of the patient will be best ensured by postponing the myomectomy till some time later, when it can be done with far less risk of shock.

There is an excellent section on postnatal examination, but it is surprising to find that cervical erosion in the postnatal patient is treated by application of mercurochrome " thrice and later twice weekly for about 6 weeks," when the erosion can be cured at one sitting by radial cauterization by the electric cautery! It is, however, a pleasure to quote Professor Strachan's opinion on the treatment of postnatal retroversion. " In our view far too much attention has been paid to retroversion and it is questionable if a simple mobile retroversion uncomplicated by inflammatory adhesions produces any symptoms .... We have met many more women who have become neurotic and introspective simply by being told, possibly many years previously that they had a displaced womb." With this statement we most heartily agree for we believe that in the past the treatment of retroversion and playing about

with pessaries for its "cure" has bulked far too largely in the routine of the postnatal clinic.

Finally, two aphorisms are worth quoting: "When a fibroid is present along with pregnancy it is the pregnancy that is apt to be overlooked, but when an ovarian cyst complicates pregnancy it is the cyst that is likely to be missed." And again: "The longer things are left to nature the less there is for the obstetrician to do." Dr. Arthur Watkins has contributed a valuable section on "The Care and Disorders of the Newborn Child", and Dr. Drummond, Transfusion Officer to the Welsh Board of Health, a very readable one on "Blood Transfusion in Obstetrical Practice." These add materially to the value of a very valuable book.

F. J. BROWNE

Expansion of Health Services in Kashmir

THE recent expansion of the Health Services of Kashmir provides medical facilities for even the most remote areas. The eighty-eight new rural dispensaries opened in 1947 provide beds for indoor patients, as well as other medical services. For every ten rural dispensaries there is a central dispensary with a large number of beds, equipped for surgical and medical treatment. These rural dispensaries also function as rural health centres and attend to sanitation, water supply, vaccination, maternity and child-welfare, nutrition, school health and the prevention of epidemics.

Three well-equipped and up-to-date hospitals were recently constructed at Srinagar, Jammu and Mirpur, provided with modern equipment and specialists who have trained outside India. These institutions serve also as training centres; those at Jammu and Srinagar have 500 beds. The opening of a Medical College in the State is contemplated.

Great progress has been made in preventive medicine. Vaccination is compulsory, and the incidence of deaths from small-pox and cholera is negligible. No cases of plague have occurred since 1938, and an Infectious Diseases hospital will shortly be opened at Srinagar.

At Tangamarg, one of the most beautiful health resorts, a well-equipped sanatorium accommodates 100 patients, and in order to segregate patients more completely the Tuberculosis Hospital at Srinagar is being expanded to accommodate 100 patients also. Expansion of the T. B. Hospital at Jammu is being undertaken.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages, and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

INDEX

ANATOMY

364. A Spiral Artery in the Ovary of the Rabbit.
By S. R. M. REYNOLDS. *Amer. J. Obstet. Gynec.*, 53, 221–225, Feb. 1947. 6 figs., 3 refs.

365. Standardized Radiological Pelvimetry. 1. Quantitative Aspects.
By E. P. ALLEN. *Brit. J. Radiol.*, 20, 45–54, Feb. 1947. 5 figs., 22 refs.

After discussing the lack of uniformity in the various methods of radiological pelvimetry the author suggests a series of 6 requirements for a standard system. (1) All significant diameters must be measured with sufficient accuracy for practical purposes. (2) The method must be capable of application to all standard apparatus. (3) Accurate description must be possible so that other workers can follow the method. (4) It should be simple and avoid complicated mathematics. (5) It should provide some basis for morphological classification of the pelvis. (6) It should be sufficiently concise to permit application by those without great experience.

The author bases his arguments and observations on the examination of 220 primigravidae and upon the results of mensuration of 12 dried pelves. The latter are all specimens of 50 years ago and 10 of them are from Maori natives. He does not suggest that the latter are fully representative of the skeleton of to-day, but he uses the results of his measurements to make certain points later in the paper. He states that it is the function of pelvimetry to investigate the clinically inaccessible lower parts of the pelvis rather than the brim, for which the foetal head remains the best pelvimeter. In discussing actual mensuration he makes a plea for accuracy and for the abandonment of those measurements relying on the identification of external bony points. With regard to the transverse measurements, he points out that all the usual ones have well-defined bony end-points, except the bituberous and the anterior transverse, and that the oblique diameters are of doubtful value if the conjugate and the transverse are known. With regard to the measurement of the true conjugate he suggests that most information can be obtained from this measurement by altering its posterior end-point according to the size of the pubosacral angle—that is, the angle formed between the classical conjugate and the plane of the anterior surface of the first sacral vertebra. Where this angle is less than 90 degrees the smallest available diameter lies below the classical conjugate and is approximately the conjugate of Caldwell and Moloy; where it is more than 90 degrees the classical conjugate gives the available diameter. In the author's experience the majority of pelves have a pubosacral angle of 90 degrees or more.

In the midplane he suggests the addition of a fourth measurement to the usual three—namely, the anterior or true transverse (between the flat opposing surfaces of the ischia anterior to the bases of the spinous processes). Although the fourth sacral segment is taken as the posterior end-point of the sagittal diameter in this plane, the more reliable end-point is the tip of the last fixed sacral segment. While the bispinous diameter is nearly always employed as the significant diameter in the mid-plane, most of the cases examined had 64 per cent of the sagittal diameter in this plane in front of the bispinous diameter, so that the available bony diameter is greater than the bispinous measurement would suggest and the head would pass easily anterior to the spines. This available diameter can be assessed by making a graphic reconstruction of the midplane at this level and then finding the anterior transverse diameter.

For the outlet he recommends the measurement of the subpubic angle by the method of Chassard and Lapine, of the bituberous diameter, and of the pubotuberous diameter. He considers the posterior sagittal of Klein to be too unreliable and too difficult to measure accurately. Of the measurements in this plane, the only one which can be made accurately is the subpubic angle, but this alone does not give full information as to the size of the outlet, and the author suggests that a further advance can be made by measuring the symphysis-biparietal distance. Two subsidiary methods of assistance are suggested, that of charting or reconstruction and that of calculation of the areas of the inlet and midplane. *P. J. Kerley*

366. Standardised Radiological Pelvimetry. II. Qualitative.
By E. P. ALLEN. *Brit. J. Radiol.*, 20, 108–118, Mar. 1947. 2 figs., 23 refs.

367. Graphic Portrayal of Relative Pelvic Size.

By W. F. MENGERT and W. C. ELLER. *Amer. J. Obstet. Gynec.*, 52, 1032–1040, Dec., 1946. 4 figs., 3 refs.

The authors consider that the methods in common use for estimating the pelvic capacity do not give a clear mental picture of the pelvis. They recommend that the approximate size and shape of the inlet, mid-pelvic, and outlet planes should be plotted on a sheet of paper on which is a graphic outline of their normal counterpart. The probable course of labour in mild degrees of disproportion can be more readily foretold if, in addition, a diagrammatic, transparent, plastic " cut-out " of small, average, and large foetal heads is superimposed on the graphic outline of the pelvic size.

Gladys Dodds

368. Recognition of Midpelvic Contraction.

By W. C. ELLER and W. F. MENGERT. *Amer. J. Obstet. Gynec.*, 53, 252–258, Feb., 1947. 5 figs., 11 refs.

In the past much attention has been paid to the anatomy and measurements of the pelvic inlet and outlet. The authors of this paper, writing from the Department of Obstetrics and Gynecology, South-western Medical College, Dallas, feel that not enough interest has yet been aroused in configuration of the midpelvic plane. Abnormalities of this plane may not infrequently account for difficult labour and for stillbirth, and lead to dangerous operations on the foetus. A plea is put forward for the study of this plane and for its more frequent estimation by radiological methods. Only when clinics have done this in more cases will it be possible to assess the frequency of mid-plane contraction and to analyze the effects on labour.

Kenneth Bowes

PHYSIOLOGY

369. Sensory Innervation of the Adnexa and Uterus. (La innervazione sensitiva utero-annessiale. Contributo alla fisiologia del sistema nervose vegatitivo nell' uomo.)

By G. PIERI. *Clin. ostet. ginec.*, 49, 1–21, Jan.-Feb., 1947. 4 figs., 20 refs.

370. Ovulation without the Formation of a Corpus Luteum in the Human Subject. (Ovulation ohne Corpus luteum-Bildung beim Menschen.)

By H. STIEVE. *Med. Klinik.*, 41, 479–482, Oct., 1946. 11 refs.

The author describes the changes in the ovarian follicle during its development and after its rupture. He believes that the granulosa cells multiply considerably before the follicle ruptures, and that immediately after the ovum is extruded vascularization occurs, the granulosa cells enlarge, and the corpus luteum is formed. As a result of secretion of the corpus luteum the endometrium undergoes changes which prepare it for the reception of the ovum.

He has on rare occasions observed cases where after the follicle has ruptured, a corpus luteum has not formed. One such case occurred in a nulliparous woman, 32 years old, who died suddenly as the result of an accident. She had menstruated for 4 to 6 days every 24 to 32 days. Her last menstrual period was on December 5th, 1943, and she died on December 29th, 1943. Postmortem examination showed a healthy woman with no signs of disease. The genital organs were normal. The endometrium was in the proliferative phase about the fourteenth to eighteenth day of the cycle. The right ovary contained numerous follicles at various stages of development and a 6-weeks-old corpus luteum of menstruation. The left ovary also had numerous follicles and a projecting dark-red mass with a small opening on the surface closed with fibrin. This mass measured 10 × 6 mm. and it was filled with coagulated blood and fluid. The inner wall of this consisted of a layer of numerous fibrocytes and collagen substance. The fibrocytes were 6 to 8 mm. long and lay either singly or in groups. Numerous mitotic figures were present. Towards the centre, around the coagulated blood, the cells were proportionately filled with a dark-brown substance. There were no ovum and no granulosa cells in the mass.

The microscopical findings resemble in some ways those seen with an atreptic follicle in which the granulosa cells have disappeared and the theca interna has reformed. The rupture point and the marked folding of the wall resemble rather a corpus luteum than an atreptic follicle. To such bodies the author gives the name " theca body " or " corpus fuscum ". The granulosa cells must all have been extruded with the ovum, corona radiata, and discus proligerus. The reason for this is not obvious, but the phenomenon is of clinical as well as scientific interest.

Gladys Dodds

371. Regular Appearance of a Specific Proteinase during Menstruation. (Ueber das regelmässige Auftreten einer spezifischeu Proteinase während des mensuelen Zyklus.)

By H. ROEMER. *Klin. Wschr.*, 24–25, 116–121, Nov. 15 and Dec. 1, 1946. 14 figs., 2 refs.

Becker-Glauch and Winkler demonstrated the presence of a specific proteolytic substance in the urine of women on certain days during the menstrual cycle. .They used a modification of Abderhalden's test and estimated quantitatively the amount of the proteinase. At the Universitäts-Frauenklinik, Giessen, the author has carried these investigations one stage further by examining daily 24-hour specimens of urine during complete menstrual cycles. He has found proteinase regularly present at definite times: just before the onset and during menstruation, and about the middle of the menstrual cycle. In 2 cases the proteinase occurred on two separate occasions during the intermenstrual period. In the remaining days of the cycle the proteinase was absent.

The time of appearance of the proteinase does not correspond with the secretory curves of the follicular or of corpus luteum hormones. The author postulates, since the proteinase is present at the middle of the menstrual cycle at the normal time of follicle rupture, either a specific ovum hormone or that the breakdown of cells discharged from the rupture of the follicle produces this specific protein. The presence of the proteinase on two occasions during the intermenstrual period would suggest that ovulation had occurred twice in that cycle. The author suggests that, as the proteinase is regularly excreted always just before or with the onset of menstrual bleeding, either it is produced by a hormone set free from the dead ovum or the hormone from the degenerating corpus luteum contains the same proteinase as that of the ruptured follicle.

This report is a preliminary one and further work is being done on the urine of pregnant and menopausal women. The demonstration of the regular physiological appearance of this specific proteinase during the menstrual cycle opens up another avenue of investigation on the cyclic hormonal control of menstruation.

G. Dodds

372. Cyclic Changes in the Physical and Chemical Properties of Cervical Mucus.

By W. T. POMMERENKE. *Amer. J. Obstet. Gynec.*, 52, 1023–1031, Dec., 1946. 1 fig., 24 refs.

Observations were made on cervical mucus throughout the menstrual cycle, except during menstruation. The mucus was obtained by aspiration from the external os and the cervical canal. The subjects investigated were young women with normal cycles and normal pelvic findings.

The maximal production of mucus occurred during the ovulatory phase, when it was 10 to 12 times the amount at other phases. The viscosity of the mucus was found to be so low in this phase that it could traverse a given distance through a capillary tube in only 2 to 3 seconds, while mucus obtained at other phases took 100 seconds to traverse the same distance under the same set of standard experimental conditions. During the ovulatory phase also, spermatozoa penetrated the mucus readily and rapidly at a rate of 3 mm. per minute, while the rate was 0.25 mm. at other phases. The water content of cervical mucus was highest in the ovulatory phase. Chemical investigations showed variations in the amount of carbohydrate and amino-acids in the mucus during the cycle. These observations suggest that the cervical mucus during ovulatory phase is the most propitious for the reception, passage, and nutrition of spermatozoa.

Gladys Dodds

PREGNANCY

Normal.

373. Biological Titration of Gonadotrophins in Obstetrics. (Titulación biológica de las gonadotropinas en obstetricia. [Trabajo de ingreso.])

By G. VILLAVICENCIO. *Bol. Soc. chil. Obstet. Ginec.*, 11, 166–183, Oct., 1946. 13 refs.

374. Estimation of Oestrone in the Urine in Pregnancy. (Le dosage de l'oestrone urinaire au cours de la grossesse.)

By C. MAYER. *Rev. franc. Gynéc.*, 41, 337–346, Nov., 1946. 27 refs.

Oestrogens are substances capable of causing keratinization of the vagina and oestrus in the castrated female rat or mouse. The basic substance is oestradiol ($C_{18}H_{22}O_2$), formed in the

ovaries. In human urine two derivatives are found: oestrone ($C_{18}H_{24}O_2$) and oestriol ($C_{18}H_{24}O_2$), The oestrogenic activity of human urine is due almost entirely to oestrone, as oestriol has only 0.9 per cent of the activity of oestrone, while oestradiol is present in negligible quantities only. There are two methods of estimating oestrone—the biological and the colorimetric. The biological method may determine either the keratinization of the vagina (as shown by the examination of vaginal smears) in the castrated rat or mouse, or the size of the introitus in the immature rat, or the increase in weight of the uterus of the immature rat or mouse. All these tests are complicated in interpretation, need a large number of animals, take 24 hours or longer, and are subject to an error of 20 per cent. The units used are also considered unsatisfactory. The colorimetric method is based on the development of a pink colour when β-naphthosulphuric acid is added to oestrone, the depth of the colour depending on the amount of oestrone (Kober's reaction). As this colour disappears on addition of hydrogen peroxide, the estimation in the urine entails a comparison of the final residual colour with a standard. The method is comparatively rapid and easy and is more accurate than the biological one. During pregnancy the amount of oestrone in the urine increases, the actual level depending on the size of the placenta. The author regrets that estimations of oestrone are not universally measured in μg. of oestrone but in rat and mouse units, the relation between the various units being: 1 mouse unit equals 8 international units; 1 rat unit equals 32 international units; 1 international unit equals one-tenth μg. He concludes this interesting article by describing his own method of preparing the urine for a colorimetric examination and by giving in detail the results in 10 cases of pregnancy on which altogether 72 estimations were performed; in 2 cases the first estimation was done as early as 6 weeks after the beginning of pregnancy, and in 7 cases the final estimation was made after labour (there being a dramatic drop in the level after delivery). In one of the cases at 3 months the amount was 620 μg. per 1,000 ml., and at 4 months only 450μg. per 1,000 ml., a miscarriage occurring 2 days after this last estimation.

Nicholas Tereshchenko

375. The Value of Plasma Pitocinase Determinations in Obstetrics.

By E. W. PAGE. *Amer. J. Obstet. Gynec.*, 52, 1014–1022, Dec., 1946. 3 figs., 19 refs.

A series of cases is recorded in which quantitative estimations have been made of an enzyme present in the blood. This enzyme destroys the oxytocic properties of pitocin and is referred to as pitocinase. From the fourth to the sixteenth week of normal pregnancy there is a 100 per cent increase in plasma pitocinase every 12 days. By quantitative estimation during this time the date of conception can be calculated to within 6 days. From the sixteenth to the thirty-eighth week there is a further increase of pitocinase, but the rate of increase is less steep than in the early weeks, so that the time of conception or of delivery cannot be accurately estimated. Pitocinase remains at a high level in the blood during labour. After delivery it decreases and disappears· in 4 weeks. Twins, triplets, and intrauterine death do not alter the quantitative values from the normal range. The placenta at term has 30 to 50 units of pitocinase per gramme of tissue. The enzyme is not present in the foetal blood. Quantitative estimations were made in 16 pre-eclamptic and eclamptic patients and no correlation was found between the amount of pitocinase and the severity of the disease. Traces of pitocinase were found in 20 non-pregnant patients. Packed red cells, after haemolysis, contained the same amounts per gramme of the enzyme as did plasma at full term, regardless of species or sex.

Gladys Dodds

376. Investigations into the Tocopherol Content of the Blood of Pregnant and Aborting Women. (Undersogelser over Tokoferolindholdet i Blod. En Sammenligning mellem Tokoferolindholdet i Blodet hos gravide og aborterende Kvinder.)

By K. FAABORG-ANDERSEN. *Nord. Med.*, 42, 2401–2404, Oct. 18, 1946. 47 refs.

A non-specific chemical method was used to study the level of vitamin E in the blood of 25 healthy pregnant women and 48 women who had aborted. The range found was 1.9 to 17.2 μg. per ml. for the healthy and 1.6 to 17.6 μg. per ml. for the patients who had aborted. There is no detectable difference between these ranges.

G. Discombe

377. Placental Toxin: Inactivation and Tolerance during Pregnancy.

By C. L. SCHNEIDER. *Amer. J. Physiol.*, 147, 255–259, Oct., 1946. 3 figs., 6 refs.

Blood contains an inactivator for a placental toxin. The present paper shows that the potency of the inactivator rises during pregnancy both in mouse and man.

Extracts of fresh placenta were used as reagents for the measurement of the inactivator. The frozen extracts were thawed, centrifuged, assayed, and diluted to appropriate concentrations. The toxic extracts used as reagents were prepared from dry placental powder; mixtures of toxic extract of pH 7.4 and different amounts of diluted serum and sufficient saline to yield an initial toxin content of 20 units per ml. were prepared, the serum being added last in each case. The inactivating potency ·in units was that dilution determined by interpolation which caused 50 per cent inactivation of the toxic extract.

The inactivator in the serum has the properties of a protein. The increase in titre began in human pregnancy after the tenth week, the maximum titre being reached just before term. Normal levels were restored a few weeks after delivery. In mice the maximum titre was also reached before term and averaged approximately $2\frac{1}{2}$ times the normal. At the same time, and in spite of the greater inactivating potency of the serum, sensitivity to the toxic extracts increased about $2\frac{1}{2}$ to 4 times during pregnancy. In contrast with non-pregnant mice, liver necrosis was encountered only rarely in pregnant mice after sub-lethal doses of toxin. The pregnant mice were not easily desensitized. However, with careful repetition and increase of dose a desensitization or refractory period could be induced. Then massive doses (20 to 40 units) given during the refractory period regularly resulted in focal liver necrosis. This response was the same as that obtained from non-pregnant mice after they had received massive doses during the refractory period, which could be induced readily by single sub-lethal doses of toxin. After treatment with massive doses the pregnant mice, like the non-pregnant ones, besides the focal liver necrosis, occasionally had blood in the small intestine, and some developed bilateral cortical kidney lesions.

The foetuses were usually dead at sacrifice if the animals had not already been aborted.

F. J. Browne

378. Desensitization of Mice to Placental Toxin.

By C. L. SCHNEIDER, *Amer. J. Physiol.*, 147, 250–254, Oct. 1946. 5 figs., 3 refs.

The placental toxin is a protein, inactivated by heating to 85°C. for 10 minutes, poorly soluble in water, and precipitated by half-saturated ammonium sulphate solution or 15 per cent alcohol in the cold. In the simple saline extracts 0.10 mg. of protein corresponded to 1 unit of toxin; for preparations reprecipitated with alcohol 0.06 mg. corresponded to 1 unit. Intravenous injections were lethal to mice while sub-lethal doses resulted in focal liver necrosis. After these single intravenous injections the sensitivity of the mice decreased. The onset of the desensitization was rapid, and in 3 minutes after the injection the mice were able to survive 7 units (7 M.L.D.); within 10 minutes they could survive more than 20 M.L.D. —that is, enough to kill more than 20 untreated mice. Within 24 hours the sensitivity had returned almost to normal. There were visible focal liver lesions in 95 per cent of the animals desensitized and afterwards treated by massive doses of toxin. Bleeding into the small intestine was not uncommon and the kidneys showed toxic changes.

F. J. Browne

379. The Kidneys and Pregnancy. (Nier en zwangerschap.)

By M. A. van BOUWDIJK BASTIAANSE. *Belg. Tijdschr. Geneesk.*, 3, 193-207, Mar. 1947.

380. The Importance of the Liver in Reproductive Physiology.

By S. J. GLASS. *West. J. Surg.*, 55, 114–119, Feb. 1947. 17 refs.

381. Experimental Study of the Passage of Sulphonamides from the Blood Serum of the Mother to that of the Foetus in the Amniotic Liquid and in the Lochia. (Contributo sperimentale allo studio del passaggio dei sulfamidici dal sangue della madre nel sangue fetale, nel liquido amniotico e nei lochi.)

By A. CARIANNI. *Ginecologia, Torino*, 13, 37-46, Jan. 1947. 5 refs.

382. The Laboratory Diagnosis of Pregnancy.

By J. BAMFORTH. *Practitioner*, 158, 154–157, Feb. 1947. 16 refs.

383. The Hogben Test in Comparison with the Determination of Chorionic Gonadotrophin by Weight in Early and Interrupted Pregnancy. (Hogbentest im Vergleich mit der gewichtsmässigen Choriongonado-tropinbestimmung bei Früh-und gestörter Gravidität.)

By C. A. JOEL. *Schweiz. med. Wschr.*, **76** 1106–1107, Oct. 26, 1946. 1 fig., 3 refs.

The results of the Hogben test, in which the clawed toad, *Xenopus laevis,* is used for the diagnosis of early pregnancy, have been compared with the results of the Aschheim-Zondek reaction and with the results of estimation of chorionic gonadotrophin by weight in the urine. Tests have been performed in early and in interrupted pregnancy. It was found that at the sixth week of pregnancy the Hogben test was still negative; it should not, therefore, be used for the diagnosis of very early pregnancy. By the seventh or eighth week the results with the Hogben test are similar to those obtained by the other two methods. In interrupted pregnancy a parallel fall in chorionic gonadotrophin excretion and in reaction to the Hogben test takes place. *Josephine Barnes*

384. An Evaluation of the Pregnancy Test Based on Ovarian Hyperemia in the Immature Rat.

By C. A. BUNDE. *Amer. J. Obstet. Gynec.,* **53**, 317–320, Feb. 1947. 6 refs.

385. Further Observations on the Two-hour Pregnancy Test.

By H. S. KUPPERMAN and R. B. GREENBLATT. *J. med. Ass. Georgia,* **36**, 58–63, Feb. 1947. 22 refs.

386. Nutrition in Pregnancy. The Effects of Dietary Deficiency in Pregnancy and the Detection and Treatment of Nutritional Deficiency Diseases.

By C. F. VILTER, D. MORGAN, and T. D. SPIES. *Surg. Gynec. Obstet.,* **83**, 561–571, Nov. 1946. 3 figs., 64 refs.

Nutritional failure is more likely to occur during the course of pregnancy and lactation than at any other period of a woman's life. Strangely enough there has been no demonstration that malnutrition has anything to do with conception in women. The same factors that operate to induce nutritional failure in any person are applicable in pregnancy —namely: (*a*) failure of ingestion of foodstuffs, (*b*) increased requirements, (*c*) interference with absorption, (*d*) interference with utilization, (*e*) increased excretion, and (*f*) increased destruction.

The first two account for most of the nutritional trouble in pregnancy.

Recommended Daily Allowances of Specific Nutrients for the Non-Pregnant, Pregnant, and Lactating Women.[*]

Nutrients	Non-Pregnant	Pregnant (latter period)	Lactating
Calories	2500	2500	3000
Protein (g.) ...	60	85	100
Calcium (mg.)	0.8	1.5	2.0
Iron (mg.)	12	15	15
Vitamin A (I.U.)	5000	6000	8000
Thiamine (mg.)	1.5	1.8	2.3
Ascorbic acid (mg.)	70	100	150
Riboflavin (mg.)	2.2	2.5	3.0
Nicotinic acid (mg.)	15	18	23
Vitamin D (I.U.)	+	400–800	400–800·

[*] Food and Nutrition Board, National Research Council, Reprint and Circular Series No. 115, 1941.

The factors predisposing to nutritional disease in the mother are the parasitic demands of the foetus, the economic status (availability does not insure an adequate dietary), nausea and vomiting of the first trimester, and multiple pregnancy. A study of 229 mothers between 18 and 45 years old at the Nutrition Clinic in Birmingham, Alabama, was made, disease symptoms being correlated with age, the time of their appearance, and the number of pregnancies. Only 4 out of 229 mothers had definite symptoms of nutritional disease before the first pregnancy, but 135 developed symptoms during lactation or pregnancy. The onset of symptoms was mostly in the third trimester, and commonest during fourth and fifth pregnancies. The mother is likely to give the food of higher quality to her husband and children, and the allotment of food for the family remains unchanged during her pregnancy. Isolated syndromes such as anaemia pellagra or neuritis are always a manifestation of a general and mixed nutritional deficiency. Treatment of the single symptom with a single specific substance without dietary control and combined therapy results in incomplete recovery.

Beriberi (polyneuritis of pregnancy) often follows

hyperemesis gravidarum and hence may appear early in pregnancy. Synthetic thiamine in doses of 5 to 20 mg. daily ameliorates the disorder. Macrocytic anaemia of pregnancy shows occasional refractoriness to parenteral treatment with liver preparations. Synthetic folic acid has recently proved effective in all varieties of macrocytic anaemia due to deficiency of liver principle, not excepting the macrocytic anaemia of pregnancy. Whether given orally or parenterally, and adequate daily dose (approximately 10 mg.) is followed by the appearance of reticulocytes in the peripheral blood and restoration of blood counts to normal. This is a rare dyscrasia in the United States.

Niacin deficiency causes in the pregnant woman the same signs and symptoms of pellagra that are found under circumstances unrelated to reproduction. There is a possibility that prenatal and postpartum psychoses might be related to deficiency of vitamin-B complex. Warkany has shown that deficiency of riboflavin during the differentiation stage of the rat embryo produced congenital abnormalities, such as " shortening or absence of ribs, digits, and extremities, shortening of the mandible, cleft palate, deformities of the eyes, and similar anomalies ". It is also responsible for angular stomatitis. Deficiency of vitamins C and K is briefly discussed. Congenital blindness is induced by vitamin-A deficiency in the calf, pig, and rat. As regards vitamin-D deficiency, it is a physiological impossibility to drain calcium from the erupted tooth, so pregnancy does not aggravate or initiate dental caries. Vitamin E is only very briefly mentioned. The causes of the anaemia are iron deficiency and chronic blood loss.

The maintenance of an adequate protein intake is a major factor in directing an efficient pregnancy. Protein deficiency, if not the initiating cause of toxaemia, is a prominent predisposing factor. The view that high protein intake induces toxaemia has given way to the view that the very opposite is true. Some investigators still believe that there is no correlation between the amount of dietary protein and toxaemia, but it is reasonably safe to say that the woman whose protein intake during pregnancy has been adequate usually does not develop toxaemia. Such a dietary includes a quart of milk, two moderate servings of meat, and one to two eggs, daily. A good supply of protein during pregnancy also ensures the best conditions for successful lactation.

The principles of treatment advised for nutritional disease occurring during pregnancy do not differ from those prescribed in non-pregnant women—namely, (a) a diet providing 3,500 to 4,000 calories, including 120 to 150 g. protein, adequate vitamins, and minerals; (b) synthetic vitamins in balanced amounts; (c) specific therapy with synthetic vitamins directed at the more prominent symptoms; and (d) a natural source of vitamin-B complex, such as brewers' yeast, crude liver extract, or wheat germ.

[In many European countries this article will have to be laid aside and resurrected when rationing ends. The apparent increase in intrauterine *death of the foetus and of cases of toxaemia may* have something to do with the long period of rationing in Britain, and, from this point of view, the opinions expressed in this paper are interesting.] G. Gordon Lennon

Abnormal.

387. **The Value of the Alkali Reserve Test in Obstetrics and Gynecology.**
By A. SADOVSKY and R. M. HEIFETZ. *Exp. Med. Surg.*, 4, 306–309, Nov. 1946. 2 refs.

Tissue anoxia due to accumulation of carbon dioxide is normally prevented by the buffer system of the blood and the alkali reserve. Diminution in the alkali reserve may be met with in vomiting of pregnancy, eclampsia and pre-eclampsia, labour (especially if prolonged), and general anaesthesia. The combination of general anaesthesia and obstetric complications may be very dangerous. Alkali reserve estimations (224) were made by the Van Slyke method in 147 cases of various obstetric complications of labour and, for comparison, in gynaecological operations (96 gynaecological cases, 18 cases of pregnancy, and 35 deliveries). In the gynaecological group only a few patients had a low reserve before operation, and in these cases operation was deferred. Ether was found to aggravate acidosis, whereas local analgesia did not. The authors therefore stress the value of the latter. The alkali reserve was lowered even in normal labour, and more markedly so if labour was prolonged. Out of 69 examinations made during delivery 34 gave values below 40 volumes per cent. In eclampsia the value fell to 28.1 volumes per

cent the day before fits and to 17.6 volumes per cent during fits. In jaundice the value was 26.6 volumes per cent. Diminution was also observed in cardiac disease complicating pregnancy.

R. K. Bowes

388. Eclampsia. Report of a Case in which there was Extensive Destruction of the Brain.

By H. JOSEPHY and E. F. HIRSCH. *Arch. Path., Chicago*, 42, 391–401, Oct. 1946. 4 figs., 13 refs.

A case of post-eclamptic cerebral atrophy in a white girl aged 15 years is described. Only one other case was found in the literature. Pre-eclampsia with its usual signs appeared at the eighth month of pregnancy and progressed until labour was induced medically. During labour the *patient had 5 generalized convulsions, and after* delivery she passed into a condition resembling status epilepticus for 45 minutes until " sodium amytal " was administered. Subsequent convulsions were similarly controlled. Eleven days after induction of labour a condition resembling decerebrate rigidity developed and persisted until the patient died 3 months later without regaining mental consciousness. The temperature varied between 101° and 104°F. (38.3° and 40°C.). A ventriculogram demonstrated the presence of cerebral atrophy. The essential finding at necropsy was the presence of flat atrophic convolutions with narrow sulci affecting more specially the frontal, temporal, and anterior part of the parietal regions. Coronal section of the cerebrum after formalin fixation showed narrowing of the cortex, which was separated from the centrum ovale by a layer of soft loose tissue. In some places the cortex was actually separated from the white matter. The latter was pale and friable, these changes being most marked in the temporal poles. The lateral ventricles were dilated but otherwise the brim was normal. Blocks of tissue were embedded and stained with toluidine blue, by van Gieson's method, and for myelin sheaths, neurofibrils, mesenchymal structures, and lipids. A detailed description of the histological changes is given, the salient points being extensive demyelination of the parietal lobe and the second and third temporal gyri, together with destruction of the cortex of the anterior parts of the cerebrum and especially the first and second frontal gyri. In the cortical lesions there was marked loss of nerve cells and fibres, the subsequent reactions being either softening with organization, or gliosis. The blood vessels were dilated and small haemorrhages were found. The basal ganglia and brain stem were normal. In the cerebellum, Purkinje cells and the cells of the dentate nucleus were considerably reduced in number.

The authors summarize their findings and point out that they observed the early stages of what was described by Lowenberg and Lossman in their case (the only other one on record), in which death occurred 7 years after the eclampsia. They review numerous reports of other less severe changes and, comparing them with their own, form the opinion that the pathogenesis of all these changes is essentially vascular, involving vasoparalysis and thrombosis of capillaries and venules. They admit that a toxic factor such as anoxaemia may be partially responsible for the demyelination of the centrum ovale.

R. B. T. Baldwin

389. Late Postpartum Eclampsia.

By H. J. STANDER, R. W. BONSNES, and W. B. STROMME. *Amer. J. Obstet. Gynec.*, 52, 765–772, Nov. 1946. 5 figs., 1 ref.

In the light of their previous experience the authors held the view that in the majority of cases postpartum eclampsia occurred within 72 hours of delivery. They have had to modify their view, however, on account of recent experience to include the first week of the puerperium. During the period from September 1st, 1932, to January 1st, 1946, there were 70 cases of eclampsia in the New York Lying-in Hospital, and of these the eclampsia occurred postpartum in 23 cases. In all but 3 of these it took place within 30 hours of delivery. The 3 late cases in which there was postpartum eclampsia respectively on the fourth, sixth, and eighth days after delivery, are recorded with full details of the clinical findings and laboratory investigations. All 3 showed the features characteristic of true eclampsia—namely hypertension, albuminuria, oedema, convulsions, elevated uric acid level and decreased carbon-dioxide combining power in the blood, decreased uric acid clearance and diminished urinary output. There was a return to normal after the eclampsia in all but one patient, who had a persistent hypertension.

T. N. MacGregor

390. Prognostic Significance of the Diastolic Blood Pressure in Eclampsia Patients. (Die prognostische Bedeutung des diastolischen Blutdruckes der Eklampsiekranken.)

By L. VACZY. *Gynaecologia*, 122, 244–251, Oct. 1946. 22 refs.

It is difficult to decide whether the course of an eclamptic case will be mild or severe. Various investigations, such as estimation of the histamine content of the urine, measurement of capillary pressure in the skin or of muscle tone, and liver function tests, have been suggested in the past but are of little use at the bedside. They require a laboratory and good technicians, and several hours must elapse before a result can be obtained. This paper shows the value of blood-pressure readings in the prognosis during the acute stage of eclampsia. The systolic, pulse, and diastolic pressure readings in 24 cases are discussed.

No prognostic significance could be attached to the systolic blood-pressure. Thus, 12 of the 24 patients had an average systolic blood-pressure of over 100 mm. Hg. and had only 3 fits, while 12 patients with an average systolic pressure of 178 mm. Hg. had more than 3 fits. Further, 7 women who had only 1 fit had a systolic pressure of over 200 mm. Hg., while 6 women who had 5 fits had a systolic pressure of less than 200 mm. Hg. The pulse pressure was also of no prognostic value. There appears to be some relation between the height of the diastolic blood-pressure and the severity of the condition. Patients with a diastolic pressure of over 100 mm. Hg. generally had more fits than those with a diastolic pressure below 100. There was no absolute connexion between the height of the diastolic pressure and the number of fits, but it could be said that when the diastolic pressure was below 100 mm. Hg. the prognosis was better than when it was above 100.

Gladys Dodds

391. Prevention and Modern Treatment of Eclampsia.

By R. NEWTON. *Med. Press.*, 217, 255–257, Apr. 2, 1947. 10 refs.

392. Principles of Treatment in Pre-eclampsia and Eclampsia.

By J. R. WILLSON. *J. Kansas med. Soc.*, 37, 553–556, Dec. 1946.

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393. Relation of the Fetus and Placenta to the Decline of Hypertension in Pregnant Rats.

By E. W. PAGE. *Amer. J. Obstet. Gynec.*, 53, 275–278, Feb. 1947. 1 fig., 19 refs.

394. Endocrine Influences Upon the Blood-pressure of Normal and Hypertensive Rats.

By E. W. PAGE and E. OGDEN. *Amer. J. Obstet. Gynec.*, 53, 150–154, Jan. 1947. 18 refs.

395. Hypertension in Pregnancy. (Hypertensie en zwangerschap.)

By M. RENAER, *Belg. Tijdschr. Geneesk.*, 3, 208–218, Mar. 1947.

396. Premature Separation of the Placenta (102 Cases). (Förtidig placentarlösning. Sammanställning av 102 fall.)

By L. IACOBAEUS. *Nord. Med.*, 32, 2509-2512, Nov. 1, 1946. 30 refs.

An analysis is given of 102 cases of premature separation of the placenta occurring in 20,640 deliveries at the Gynaecological Clinic, Lund. The cases are grouped according to severity of symptoms; 22 were mild, 49 moderately severe, and 31 very severe or fulminating. It has been suggested that the condition tends to occur more frequently in the higher age-groups, but this was not so in the series under analysis. There was a higher proportion of severe or fulminating cases among multiparae. Only 54 per cent showed albuminuria or other evidence of renal lesion, while only 12 of the patients had had a previous abortion. Nearly 60 per cent of the cases occurred at full term and 30 per cent in the ninth month. One case was definitely precipitated by attempted version for a foetal malposition.

Mild cases need no special treatment. In more severe cases delivery must be effected either naturally by forceps, or by vaginal or abdominal Caesarean section. Suitable adjuncts such as blood transfusion are used as indicated. The severity of symptoms and general condition of the patient determine the need for intervention, and no rule can be laid down for any given case. There were 9 vaginal and 17 abdominal Caesarean sections. Hysterectomy was not performed in any case. The maternal mortality was 2 per cent. Immediate foetal mortality—that is when the child was dead on arrival or died during delivery—was 53 per cent, but if the immediate postnatal period is included it was 63 per cent.

J. W. S. Lindahl

397. **Placenta Accreta Found at Caesarean Section for Placenta Previa, with Preservation of the Uterus.**
By W. F. SHANNON and C. F. DODENHOFF. *Amer. J. Obstet. Gynec.*, 53, 326–328, Feb. 1947. 7 refs.

398. **Obstetric Hemorrhage, Incidence and Management. A Two-year Study (July 1, 1943, to July 1, 1945.)**
By W. R. PAYNE. *Sth. med. J.*, 40, 161–166 Feb. 1947.

399. **Ten Years' Statistics of Abortion.** (Et 10-aars abortmateriale.)
By T. KAERN. *Ugeskr. Læg.*, 109, 169–173, Feb. 13, 1947. 3 figs., 12 refs.

An analysis is made of 3,007 cases of abortion admitted to the St. Joseph Hospital, Copenhagen, between 1935 and 1945. Of these, 2,313 were early cases (up to the fourth month of pregnancy) and 694 late cases (fourth to seventh month of pregnancy inclusive). The abortion followed an afebrile course, in that the rectal temperature never reached 38°C., in 61 per cent of cases and a febrile course in 39 per cent. The mortality was 0.5 per cent and morbidity (conditions associated with the abortion) 28 per cent; the latter figure is is subdivided into 35 per cent of febrile cases and 23 per cent of afebrile cases. Active treatment was necessary in 87.1 per cent of all cases; 94.2 per cent of early cases were so treated but only 63.8 per cent of late cases

Aetiology is not discussed. The number of cases has increased steadily each year and has nearly trebled itself in the last decade. The proportion of abortions to live births is approximately the same for all age groups, but is greater in multigravidae. Approximately one-third of the patients were unmarried, and in these there was a slightly greater tendency to a pyrexial course. Of the 16 deaths, 10 were due to septicaemia (5 married, 5 unmarried), 4 to peritonitis (3 unmarried; 2 with a uterine perforation), 1 to peritonitis following an operation for salpingitis, and 1 to pulmonary embolism. The author thinks that between 80 and 90 per cent of the abortions had been induced.

S. S. B. Gilder

400. **The Obstetric Point of View in the Classification of Premature Births and Abortions.** (Obstetriska synpunkter beträffande nomenklaturen förtidsbörd abort.)
By C. VON NUMERS. *Nord. Med.*, 32, 2745–2750, Nov. 29, 1946. 2 figs.

The limit between premature and mature birth weights is now generally fixed at 2,500 g., but a limit of foetal weight dividing premature birth from abortion has not been fixed. Henderson considered that a birth-weight of 1,250 g. should represent the lower limit for premature infants, and advocated the term pre-viable to describe infants with a lower birth-weight than this.

The present author discusses the results of his survey of the relation between birth-weight and chance of survival in a total of 2,642 infants, all of whom weighed under 2,500 g. at birth. The infants were classified in 19 groups with birth-weights from 600 g. to 2,500 g. In the lowest groups (600 to 900 g.) none of the 158 infants survived the first year of life. Ten of the 395 infants (28 per cent) in the next 5 groups (900 to 1,400 g.) were still alive after one year; and in the next group (1,400 to 1,500 g.) 13 out of 80 children (16.3 per cent) survived. In the group from 1,200 to 1,300 g., which includes Henderson's limiting value of 1,200 g., the average length at birth was 38.4 cm., and the average duration of pregnancy had been 206.7 days (29.5 weeks). The average weight of all infants born between the twenty-seventh and the thirtieth weeks of a pregnancy was 1,296 g. Thus the figure of 1,250 g. agrees fairly well with the old concept of viability in which a birth before the twenty-eighth week of pregnancy was considered to be an abortion.

After the author's paper it was officially decided by the Paediatric and Gynaecological Associations of Finland that for purposes of classification: (1) infants with a birth-weight between 1,250 g. and 2,500 g. will be referred to as premature; (2) infants with a birth-weight between 600 and 1,250 g. will form a special class and will probably be called immature infants; and (3) foetuses with a birth-weight below 600 g. will be considered to be the products of abortion.

S. S. B. Gilder

401. **A Study of the Pathology of Habitual Abortion.** [In English.]
By B. FALCONER. *Acta obstet. gynec. scand.*, 26, 496–524, 1946. 8 refs.

The author analyzes 33 cases classed clinically as habitual abortion. Four cases were excluded from the discussion, as a normal pregnancy between a number of miscarriages had occurred in each.

Various causes were found to account for 14 of the remainder. Previous operation for ovarian cyst and fibromyomata accounted for 4. The presence of a uterus bicornis and a myoma was responsible for 2 more, and " tubal contractions " for another. Abnormal sperm counts were considered to point to the aetiological factor in a further 3. In the remaining 4 patients endometrial abnormalities were present: typical cystic glandular hyperplasia in 1, inactive tuberculous endometritis in 1, and dilated and cystic glands in a further 2. No evidence of an abortifacient element was found in the remaining 15 cases, and the author considers it reasonable to assume an immunobiological cause in some. He stressed the negative findings with regard to endometritis, but considers the presence of cystic glandular hyperplasia to be of particular interest.

[Defective spermatogenesis is a new observation in repeated miscarriages, and may well be the cause of " the blighted ovum ". But how it is to be treated?]

Braithwaite Rickford

402. **Fifteen Years Study of Abortion with Special Reference to Treatment.** (Et 15-ars abortmateriale —med saerlig henblikk pa behandlingen.)
By O. W. TENFJORD. *Nord. Med.*, 33, 615-620, Mar. 7, 1947. 2 figs., 15 refs.

403. **Prevention and Treatment of Abortion.**
By L. M. JEFFRIES. *Med. Press.* 217, 317-319, Apr. 16, 1947.

404. **A Simple and Rapid Method of " Approximate Dosage " of Gonadotrophic Hormones in Pregnancy.** (Su di metodo simplice e rapido di " dosaggio approssimato " delle gonadotropine gravidiche nella pratica clinica corrente.)
By A. MASCIO. *Clin. Ostet. Ginec.*, 48, 225-234, Nov.-Dec., 1946.

The object of the present work is to discover a simple and rapid means of estimating approximately the quantity of gonadotrophic hormone in serum and urine, with especial reference to such pathological conditions as hydatidiform mole, chorionepithelioma, and intrauterine death of the embryo. A modification of the Brindeau and Hinglais quantitative Friedman test is used. Only two test animals are generally necessary.

The condition of the test animal is important, and the author prefers to use rabbits about 3 months old and weighing 1,800 to 2,200 g. A preliminary laparotomy is performed to ascertain the state of the ovaries and to exclude any gross abnormality such as hermaphroditism. For the performance of the test it has been found that serum is to be preferred to urine. The use of urine has several disadvantages—excessive dilution of hormone, delay in the appearance of the reaction, toxicity of urine, and the possibility of nonspecific positive reaction. Serum, on the other hand, can be collected at any time of the day, and the gonadotrophins are less labile; the content of gonadotrophin is similar to that in urine and more constant, hence it is better for quantitative determination. The unit of gonadotrophic activity is that proposed by Brindeau and Hinglais (U.B.H.) and is defined as " the least quantity of hormone which will, after one intravenous injection in a 2-kg. rabbit, produced within 48 hours a blood spot in one of the ovaries." The author quotes the paper by Brindeau and Hinglais, giving the significance of the quantitative estimations as follows. The presence of 750-1,500 U.B.H. per litre indicates a hypoactive placenta (tendency to abortion or intrauterine death). Fewer than 500 units indicates death of the embryo. A level of 1,500 to 25,000 U.B.H. occurs in pregnancy with normal placental activity and 25,000 to 50,000 U.B.H. in toxic pregnancy with normal embryonic development, as in hyperemesis gravidarum, and 60,000 U.B.H. or over in hydatidiform mole.

The author describes certain points from his own technique. He uses two animals and aims at establishing a " liminal positive reaction." In cases of suspected hydatidiform mole the serum is diluted to 1 in 30 and 1 ml. and 0.5 ml. are injected by the intravenous route. If both tests are negative, it is assumed that the serum contains under 30,000 U.B.H. per litre and the diagnosis of living hydatidiform mole is doubtful. Similar methods are applied to cases of threatened and missed abortion and to other pathological conditions associated with pregnancy. The method has proved of practical use and a valuable aid in diagnosis.

Josephine Barnes

405. **Placental Hormones after Death of Foetus with Viable Placenta.**
By B. ZONDEK. *Lancet*, 1, 178-179, Feb. 1, 1947. 5 refs.

After expulsion of the placenta the pregnancy reaction of the urine normally remains positive for 8 days. When a positive pregnancy reaction becomes repeatedly negative it is proof that placental function has ceased, and the foetus is dead. But it is insufficient in diagnosing foetal death to rely on the negative result of only 1 pregnancy test, especially in the later months when the excretion of gonadotrophic hormone decreases and becomes less regular than in the early months. In the present paper the author presents evidence that the placenta can continue to excrete hormones for several weeks after the foetus has died and records 2 illustrative cases.

In the first case the patient was 8 months pregnant; foetal movements had ceased for 10 days when she was first seen on October 25th. No foetal heart sounds were heard and death of the foetus was diagnosed. Yet on November 12th the urine contained 10,000 rat units (R.U.) of follicle-stimulating hormones and 5,000 R.U. of luteinizing hormones per litre. On November 15th the amounts were respectively 1,000 and 500 R.U. A positive pregnancy reaction can generally be elicited with 1 or 2 ml. of urine—that is, with a gonadotrophin level of 500 R.U. per litre, so that 10 times this amount was present in this patient on November 12th. In the second case the foetus died in the eighth month. The serum-oestrone level was nevertheless high (500 mouse units per litre), thus suggesting that the foetus was alive. Three days later the patient expelled a foetus in such an advanced stage of maceration that it must have died 2 or 3 weeks earlier.

Spielman et al. had shown (J. Amer. med. Ass., 1933, 101, 266) that after extinction of placental function oestrogenic hormone disappears from the blood more rapidly than does gonadotrophin from the urine, and they therefore considered the disappearance of the oestrogenic hormone from the blood to be reliable evidence to foetal death. These cases demonstrate that even if the foetus dies the placenta can sometimes function normally and remain anatomically intact and in communication with the maternal circulation for as long as 4 weeks. In case 1 the placenta, analyzed for oestrogenic and gonadotrophic hormones, showed very low levels as compared with that of a living foetus, and the author therefore concludes that if the

foetus is dead the entire hormone output of the placenta is taken up by the maternal circulation. These observations indicate that death of the foetus can be either primary—that is, independent of the placenta—or secondary—due to death of the placenta. Whereas in secondary death of the foetus the hormone levels in blood and urine fall rapidly, in primary death of the foetus there is no such immediate fall and the levels may even rise temporarily.   *F. J. Browne.*

406. The Biological Estimation of Sex Hormones in the Pathogenic and Therapeutic Study of Habitual Abortion. (Le dosage biologique des hormones sexuelles dans l'étude pathogénique et thérapeutique de l'avortement habituel.)

By J. THOMAS-THONNART. *Rev. méd. Liège,* 2, 154–157, Mar. 15, 1947.

407. The Significance of Cervical Insertion of the Placenta in the Aetiology of Abortion and of Cervicovaginal Fistula. (Von der Bedeutung der zervikalen Insertions der Plazenta in der Abortätiologie und die der zervico-vaginalen Fistelbildung. (Fistula cervicis uteri laqueatica.)

By O. KANNEL. *Acta obstet. gynec. scand.*, 26, 610–626, 1946. 4 figs.

Cervical implantation of the placenta praevia is uncommon. The author has found 50 such cases described in the literature, 2 of which were Finnish. Implantation may be primary or secondary; probably many of the former type lead to miscarriage and therefore are never recognized The author describes 4 patients seen in early pregnancy with vaginal bleeding, in whom the placental tissue was found in the region of the external uterine os. He has also had 2 cases, both of the secondary type, in which the condition was diagnosed as placenta praevia and Caesarean section was undertaken; only then was the cervical implantation recognized. Both these patients were of the older primigravid group, and in one much of the uterine cavity was distorted by fibroids. Hysterectomy was performed after Caesarean section on account of the uterine pathology in the one case, and because of marked bleeding from the placental site in the other. Microscopy showed the erosion of chorionic villi in the cervical area. The author suggests that this erosion from undiagnosed cervical implantation of the placenta may be a cause of the rare cervico-vaginal fistula.

Kenneth Bowes

408. The Value of Hormonal Diagnosis in Hydatidiform Mole and Chorionepithelioma. [In English.]
By S. GENELL. *Acta obstet. gynec. scand.*, **26**, 555–564, 1946. 52 refs.

The author has investigated the concentration of urinary gonadotrophin in 62 cases of normal pregnancy, 31 cases of hydatidiform mole, 11 cases of chorionic carcinoma, and 31 cases of hyperemesis gravidarum. His results do not accord with the original belief of Zondek that a diagnosis of hydatidiform mole and chorionic carcinoma was confirmed by the finding of high titres of gonadotrophin. The results in normal pregnancy gave figures between 1,000 and 50,000 units per litre. The figures for hydatidiform moles were often below 1,000, while over a third of the cases showed less than 10,000 units. (Half of the normal pregnancies investigated had between 10,000 and 50,000 units per litre.) With chorionic carcinoma the figure was usually less than 10,000; in fact, not greater than with a normal pregnancy. The highest figures were obtained when hyperemesis gravidarum complicated pregnancy, over one-third of the cases giving values of between 100,000 and 300,000 units per litre. The literature on this subject is extensively reviewed.

Braithwaite Rickford

409. Report of Two Unusual Cases of Hydatid Mole.
By L. GOHSTAND. *Med. J. Austral.*, **1**, 434(b)–435, Apr. 5, 1947. 3 refs.

410. Case of Ovarian Cyst in Connection with Delivery. [In English.]
By I. VIKBLADH *Acta obstet. gynec. scand.*, **27**, 11–16, 1947. 22 refs.

411. Pregnancy Complicated by Double Uterus, Cervix, and Vagina.
By J. KLEIN. *Amer. J. Obstet. Gynec.*, **53**, 321–323, Feb. 1947. 2 refs.

412. Abnormal Hypertrophy of the Breasts in Pregnancy. (Sulla abnorme ipertrofia mammaria gravidica.)
By L. CUSMANO. *Ginecologia*, **12**, 189-200, July-Aug. 1946. 2 figs., 22 refs.

Abnormal hypertrophy of the breasts in pregnancy is due to an excessive development of the breast glands—an exaggeration, as it were, of their normal changes. Sixteen cases of this rare affection have been published since 1943. To these the author adds a case of his own, and discusses the differential diagnosis and pathogenesis.

A 35-year-old multipara noticed abnormal painful swelling of her breasts from the third month of pregnancy. A similar though lesser swelling had occurred during her two former pregnancies, but had subsided soon after abandonment of breast-feeding. Clinical and laboratory findings were normal. On examination there was an enormous symmetrical enlargement of the breasts, which reached the inguinal folds. The temperature of the breasts was raised, the surface smooth and of a uniform hardness without any isolated glandular swellings. Deep palpation caused no pain; a few drops of a dense milky fluid could be squeezed out. There were no enlarged axillary lymph nodes. Two days after a normal confinement the onset of milk secretion was marked by acute breast pain, increased local temperature, and a still greater turgor of the breasts. Owing to the formation of the nipples it was possible to extract only a few drops of milk. Attempts at breast-feeding had to be abandoned, and an incipient mastitis was successfully treated with ichthyol dressings. In the absence of any other treatment regression of the swelling was immediate, until, 3 months after confinement, the size was almost normal.

In the diagnosis of abnormal hypertrophy of the breasts in pregnancy, the following points were considered: the history of the two former pregnancies, the bilaterality of the condition, the uniform and progressive enlargement of the breasts beginning in the early months of pregnancy, the absence of nodules and lymph-node enlargement, and the good general condition of the patient. There are cases in which the differential diagnosis from bilateral lymphoblastoma is difficult. The bilateral and uniform development, though characteristic of hypertrophy, cannot exclude a neoplastic factor. It is presumed that these cases of abnormal hypertrophy of the breast are due to a hypersecretion of follicular hormone. Normally the development of the breast in pregnancy is due to two hormonal factors; one which develops the ducts (folliculin), and another which develops the acino-lobular system (lutein). For the establishment of milk secretion it is necessary for these two hormones to cease to exert their influence and for a third hormone—galactin—to appear. Cases have been

observed in which the hypertrophy reappeared in 2 to 5 successive pregnancies. Spontaneous regression of the hypertrophy is so frequent that intervention is rarely indicated. The logical treatment is the giving of androgens, which inhibit the effect of folliculin and arrest the hypertrophy. Even in high dosage up to 300 mg. androgens have not been found to harm either the pregnancy or the foetus. Breast-feeding is usually impossible in these cases and, provided that it is avoided, regression of the breasts to normal is usually speedy.

Hilde Eisner

413. Chronic Vasomotor Rhinitis in Pregnancy.
By S. L. Fox. *Bull. Sch. Med. Maryland*, 31, 104–107, Jan. 1947. 4 refs.

414. Ileus in Pregnancy. (Ileus vid graviditet.)
By E. von Post. *Nord. med.*, 33, 744–748, Mar. 21, 1947. 55 refs.

415. Carcinoma of the Rectum and Childbirth. (Carcinoma del retto e stato puerperale.)
By L. Molinego. *Ginecologia, Torino*, 13, 17–36, Jan. 1947. 13 refs.

416. Perforated Carcinoma of the Large Intestine Complicating Pregnancy. Successful Operative Management.
By W. B. Swartley, Z. B. Newton, J. C. Hartman, and J. W. Stayman. *Ann. Surg.*, 125, 251–256, Feb. 1947. 3 figs.

417. Complete Heart Block in Pregnancy. (Report of Two Successful Deliveries.)
By T. J. Quintin. *Canad. med. Ass. J.*, 55, 600–601, Dec. 1946. 1 fig., 6 refs.

Complete heart block is a rarity among pregnant women, 14 cases only having been recorded up to 1938. The author describes a patient who had two normal pregnancies and confinements. Symptoms were negligible except for slight dyspnoea on exertion during the last 2 months before the second confinement and some giddiness after stooping. Laboratory investigations did not reveal the cause of the heart block.

Braithwaite Rickford

418. Acute Leucemia and Pregnancy. Report of Fatal Case Treated with Penicillin.
By R. Harris, I. G. Tchertkoff, and L. Greenwald. *Amer. J. Obstet. Gynec.*, 53, 142–149, Jan. 1947. 3 figs., 16 refs.

419. Pregnancy and Sickle-cell Anemia.
By R. E. Martinak. *Amer. J. Obstet. Gynec.*, 53, 332–334, Feb. 1947. 7 refs.

420. Diabetes Mellitus in Pregnancy. (Om forløbet af diabetes mellitus i graviditeten. Et tilfælde af coma diabeticum med excessiv acidose efterfulgt af normoglykæmi og aglykosuri efter fødselen.)
By V. P. Petersen. *Nord. med.*, 33, 539–541, Feb. 28, 1947. 13 refs.

A 32-year-old woman had a history of two stillbirths, one due to development of a contraction ring, the other to foetal asphyxia. Her third pregnancy was normal until the seventh month, when she suddenly developed thirst and polyuria and went into coma a week later. She had a profound acidosis, plasma bicarbonate being reduced to 2.4 millimols per litre; there were sugar, protein, and acetone in the urine, and the blood sugar was 330 mg. per cent. Treatment with isotonic sodium bicarbonate solution, insulin, and glucose relieved her coma, and she gave birth to a macerated foetus. Immediate improvement in her diabetes ensued, the blood sugar returning to normal and the sugar disappearing from the urine. However, 18 months later, diabetes developed. Similar cases of transient diabetes occurring in pregnancy are referred to, the author pointing out the tendency for the condition to be associated with acidosis and coma in late pregnancy. The possibility that foetal death was the factor precipitating coma in this case is discussed.

S. S. B. Gilder

421. Pelvic Osteo-articular Tuberculosis and Pregnancy. (Tuberculosi osteo-articolare del bacino e gravidanza.)
By T. Teresio. *Ginecologia*, 12, 201–217, July-Aug. 1946. 2 figs., 27 refs.

Pelvic osteo-articular tuberculosis is rare, and its occurrence as a complication of pregnancy is exceptional. A secondary tuberculous osteitis is followed by invasion of a pelvic joint. Predisposing causes, according to some authors, are the increased genital activity during pregnancy (and puberty), the lessened resistance to infection at this time, the disturbed endocrine balance, the tendency to decalcification, and a number of traumatic factors, including those accompanying birth.

Considering the extreme rarity of the disease, the nearly simultaneous observation of 2 cases by

the author is of interest. The cases reported so far in the literature mostly concern multiparae, already known to have tuberculosis of bones or lungs, and in whom pregnancy was responsible only for a secondary localization of the disease in the pelvis. In contrast, the 2 cases observed by the author occurred in primiparae with no history of tuberculosis. As a rule the disease has no harmful influence on the course of the pregnancy. Only in exceptional cases, usually complicated by tuberculosis of the spine, is interruption of the pregnancy necessary, owing to the reduced volume of the abdominal cavity with circulatory and respiratory disturbances.

The influence of pregnancy on the course of the pelvic osteo-articular tuberculosis is disastrous, particularly when the first manifestations of the disease appear in the early months of pregnancy. In Case 1 the tuberculous lesion, localized in the left sacro-iliac joint, was already evident in the third month, while the tuberculous lesion of the os pubis in Case 2 caused symptoms in the last weeks of pregnancy. In the first case the condition of the patient became progressively worse in the second half of the pregnancy, and more so in and after the puerperium; the second case was then clinically healed. Neither before nor after confinement was it possible to detect a primary active focus from which the tubercle bacilli may have entered the blood stream to settle in the pelvis. Possibilities are the spread from a lymph node or the " flare-up " of a clinically silent tuberculosis of the pelvic bone. Among the causes predisposing to osteo-articular pelvic tuberculosis during pregnancy the diminution of the calcium content of the blood serum deserves particular attention. The localization in the pelvis may also be favoured by a decalcification of its bones.

Treatment in both cases consisted of a generous diet with the giving of calcium and vitamins and the use of ultraviolet irradiation. The author discusses the question of interruption of pregnancy in these cases. Where the patient's condition is deteriorating or the tuberculous process appears to be spreading, interruption is indicated if pregnancy is in a relatively early stage. The most satisfactory method of interruption is by the use of X-rays. Operative interference is deprecated on account of the possibility of disseminating the tuberculosis.

The condition occasionally has an unfavourable influence on the confinement, but more often the effect of the lesion on the pelvic joints leads to easier confinement. With regard to the effect of the confinement on the tuberculosis, cases are seen in which a flare-up of the disease has occurred early in the puerperium, and occasionally a miliary tuberculosis has followed. Rupture of the pelvis with a fatal outcome has also been known to occur.

Hilde Eisner

422. **Development of Pulmonary Tuberculosis after childbirth.** (Evolución de la tuberculosis pulmonar después del parto.)
By V. M. AVILES, F. RODRIGUEZ, J. ONETO, and H. AMPUERO. *Bol. Soc. chil. Obstet. Ginec.,* 11, 145–166, Oct., 1946. 9 figs., 15 refs.

423. **Pregnancy and Renal Tuberculosis.** (Gestacion y tuberculosis renal.)
By L. TISNE BROUSSE. *Bol. chil. Obstet. Ginec.,* 11, 204–211, Oct. 1946.

424. **On Miliary Tuberculosis in Association with Pregnancy and Delivery or Abortion.** [In English.]
By P. LUNDSTRÖM. *Acta obstet. gynec. scand.,* 27, 84–93, 1947. 29 refs.

425. **Pregnancy and Typhoid—Paratyphoid Fever.** [In English.]
By H. SAURAMO. *Acta obstet. gynec. scand.,* 27, 58–69, 1947. 14 refs.

426. **Ectopic Pregnancy as a Diagnostic Problem.** (A Study of 100 Cases.)
By H. B. ATLEE. *Canad. med. Ass. J.,* 56, 268–273, Mar. 1947.

427. **Combined Extrauterine and Intrauterine Pregnancy.**
By L. GRUENEWALD. *Amer. J. Obstet. Gynec.,* 53, 341–342, Feb. 1947. 1 ref.

428. **Ectopic Decidual Reaction.** (Reacción decidual ectópica.)
By A. MARANO. *Arch. Soc. argent. Anat. norm. patol.,* 8, 213–217, 1946. 4 figs., 13 refs.

429. **Early Form of Secondary Abdominal Pregnancy.**
By A. J. KOBAK and M. A. LaIUPPA. *Amer. J. Obstet. Gynec.,* 53, 329–330, Feb. 1947, 1 fig,

430. **Abdominal Pregnancy.**
By H. F. BURKONS. *Ohio. St. med. J.,* 43, 161–164, Feb. 1947. 17 refs.

431. An Analysis of 212 Consecutive Cases of Ectopic Pregnancy.

By B. LEFF and S. G. WINSON. *Amer. J. Obstet. Gynec.*, 53, 296–299, Feb. 1947. 6 refs.

432. Maternal Pulmonary Embolism by Contents of the Amniotic Fluid.

By C. T. HEMMINGS. *Amer. J. Obstet. Gynec.*, 53, 303–306, Feb. 1947. 7 refs.

433. Observations on Rupture of the Uterus.

By H. H. CAFFEE. *Sth. med. J.*, 40, 189–191, Feb. 1947.

See also Nos. 376, 455.

LABOUR

434. *Is Artificial Rupture of the Membranes to Induce Labour Useful?* (Ist die künstliche Blasensprengung als geburtsförderndes Mittel brauchbar?)

By H. SCHERER. *Gynaecologia, Basel,* 122, 233–243, Oct. 1946.

When artificial rupture of the membranes is carried out in cases of contracted pelvis several days may elapse before the onset of labour. This time interval may be shortened when the uterus is sensitized before the membranes are ruptured. *The author believes: (1) that the bag of membranes plays no part in the dilatation of the cervix; (2)* that increased intrauterine pressure stretches the uterine wall, causing spasm of the muscle fibres so that the dilatation of the cervix by retraction of the lower uterine segment either ceases or is enormously lengthened, and labour does not progress; and (3) that decrease in intrauterine pressure in suitable cases is followed by rapid delivery.

The conditions which must be present if artificial rupture of the membranes is to be successful are: (a) no obvious disproportion between the foetus and the mother's pelvis; (b) the presenting part in the inlet; (c) no vaginal infection; (d) the cervix taken up and at least one finger dilated; and (e) the uterus irritable. These conditions are often difficult to obtain, and experience is necessary before it is possible to say whether rupture of the membranes will be useful in particular cases.

The three conditions in which this method is especially useful are: (1) post-maturity, especially in multiparae; (2) over-distension of the uterus with hydramnios, twins, or a large infant; and (3) uterine inertia associated with hypertonic uterus and feeble uterine contractions. In 77 out of 79 patients in group (1) artificial rupture of membranes resulted in labour within 6 hours. In the 2 remaining patients, the estimated date of delivery had been miscalculated and they were delivered, after 30 hours in 1 case and 6 days in the other, of premature infants. In group (2) there were 30 successful cases, labour starting within 6 hours. In group (3) there were 33 successful cases with delivery mainly within 2 hours after rupture of the membranes. The author states in conclusion that while he believes that with careful assessment of all the facts artificial rupture of the membranes is the most certain method of treatment in these groups, he does not rely on one method alone in the management of his cases.

Gladys Dodds

435. The Intrauterine Use of Sulfanilamide.

By A. SADOVSKY, Y. M. BROMBERG, and Z. POLISHUK. *Exper. Med. Surg.*, 4, 310–318, Nov. 1946. 4 figs., 8 refs.

Investigations on the absorbability of sulphanilamide from the uterus were made on cases of Caesarean section, of incomplete abortion, and of curettage of various lesions. The degree of absorption proved to be greatest after Caesarean section and least after curettage and compared very favourable with the degree of absorption from surgical wounds. Local bacteriostasis was also examined by comparison of cultures in cases of local uterine sepsis. Out of 10 specimens growing *Staphylococcus aureus* and *albus* initially, 7 were sterile 24 hours later. Clinical application of this fact was made in a further series of suitable cases, and the authors conclude that the results showed the prophylactic as well as the curative value of sulphanilamide.

R. K. Bowes

436. Dichorial Unilateral Tubal Twins.

By R. S. HAUKOHL, and W. A. D. ANDERSON. *Amer. J. Obstet. Gynec,* 53, 338–339, Feb. 1947. 1 fig., 12 refs.

437. Monovular Twins.

By G. H. PICKERING. *Brit. med. J.*, 2, 988, Dec. 28, 1946.

The author records a case of twin labour which in his opinion refutes the theory of X and Y

chromosomes. The first twin, a girl, was born spontaneously and weighed 5 pounds 2 ounces (2.31 kg.) at birth; the second twin, a boy weighing 6 pounds 12 ounces (3.06 kg.), was delivered by forceps on account of deep transverse arrest of the head. Examination of the afterbirth, which came away normally after the birth of the second twin, disclosed a single bag of membranes containing 2 placentae. Detailed examination showed that there was no communication between the placentae, nor was there any evidence that there had been any fusion of the 2 gestation sacs.

T. N. MacGregor

ANAESTHETICS, ANALGESICS.

438. **Effects of Demerol in Obstetrics.**
By W. M. MALLIA. *N. Y. St. J. Med.*, 46, 2753–2756, Dec. 15, 1946. 11 refs.

Over a period of 2½ years 220 patients were given " demerol " (pethidine) with various other drugs for the production of amnesia in labour. The results were excellent in 65 per cent of cases. The drug most favoured in combination with demerol was scopolamine. Barbiturates had a depressant action on the maternal respiratory system, though no actual fatality occurred. Intramuscular injection of demerol, 2 ml. 2-hourly, and of 1/200 gr. (0.32 mg.) scopolamine 3-hourly was the routine administration. In short, rapidly progressing labours intravenous injections were given of 2 ml. demerol and 5 minutes later of 1/100 gr. (0.65 mg.).) scopolamine, and 1 hour later an intramuscular injection of scopolamine. Premedication for Caesarean section by demerol and scopolamine was also tried; the effect was good if local analgesia followed (with general anaesthesia after this premedication there were disastrous foetal results). In a subsequent discussion of this paper it was pointed out that with such a technique all patients need careful nursing and watching as there was reduced mental alertness.

R. K. Bowes

439. **The Critical Analysis of 250 Deliveries Under Continuous Caudal Analgesia.**
By J. H. PRINCE. *Ohio St. med. J.*, 43, 274–275, Mar. 1947.

440. **A Statistical Study of Delivery with Continuous Caudal Analgesia, as Compared with Other Methods.**
By S. D. COLLINS, F. R. PHILLIPS, and D. S. OLIVER. *Publ. Hlth. Rep., Wash.*, 51, 1713–1735, Nov. 29, 1946. 14 figs., 28 refs.

The authors are statisticians in the United States Public Health Service. With the collaboration of clinical colleagues they have assembled data referring to the use of continuous caudal analgesia in 2,516 mothers delivered in the Philadelphia Lying-in Unit of the Pennsylvania Hospital, between May 1943, and August 1945. Of these patients 82.2 per cent obtained complete relief without any supplementary analgesic, a further 8.2 per cent had complete relief with supplementary analgesics, 4.3 per cent received partial relief, and 5.3 per cent experienced no relief. The average duration of caudal analgesia in the series is recorded as 3 hours, with a statistical median of 2.2 hours. One-third of the mothers showed a marked drop in systolic blood-pressure after analgesia was started. The average blood loss was 127 ml. and 8.6 per cent of the patients lost more than 250 ml.

An attempt is then made to compare the results with a control series of 1,024 mothers delivered in the same hospital between December 1942, and July 1943. After analysis of the incidence of complications in the two series the authors conclude that a comparison is justifiable. They demonstrate operation rates of 84.5 per cent in the caudal analgesia group and of 69 per cent in the control series. This is mainly accounted for by an increase in the use of outlet forceps from 56.4 to 68.3 per cent. The third stage of labour was shorter in the caudal analgesia series by a statistically significant figure, and the incidence of febrile maternal morbidity was also significantly lower. Stillbirths and neonatal deaths were less frequent in the patients receiving caudal analgesia, the total loss being 20.6 per 1,000 live births in the caudal analgesia series as against 45.6 per 1,000 live births in the control series—a difference of statistical significance. Maternal deaths in each series (2 in each) were too few to permit of profitable comparison. The authors conclude that there was no evidence of danger to the mothers delivered under caudal analgesia despite the increased incidence of operative delivery, and that the outlook for the foetus is

favourably influenced by the use of this method.

[Although the mathematics of this analysis are sound, the conclusion that the better results are due to the use of the method cannot be accepted. The control series is not synchronous with the other. While the authors claim that the patients receiving caudal analgesia represent " an unselected group except for the inclusion of a few with heart disease ", no reference is made to the numbers of patients in the Philadelphia Lying-in Hospital not submitted to caudal analgesia at the time of the study, and it seems probable that some form of selection must have existed. The " controls " are loaded unfavourably in respect of foetal mortality, reference to the authors' tables indicating a proportion of babies weighing less than 4 pounds 8 ounces (2 kg.) considerably higher in the control series than in the cases under investigation, although the incidence of babies weighing 5 pounds 8 ounces (2.46 kg.) and less is similar in both series. Furthermore, while the incidence of complications arising during pregnancy and during delivery is approximately the same in both series, the detail of the complications is not analyzed in this paper. The numbers are comparatively small in both series, and important loading of one or other with an unusual incidence of such complications as placenta praevia, accidental haemorrhage, or foetal monstrosity might well have occurred. It is also permissible to speculate whether the extremely careful attention which the caudal analgesic patients were given during the investigation might not have been expected *per se* to contribute to slightly improved results. Nevertheless, the article is a reassuring contribution to our knowledge, in that it records very good results in respect of foetal and maternal mortality and morbidity obtained by a method which gives a high incidence of relief of pain at the expense of an increased incidence of operative delivery. Most British practitioners would consider the rate of operative delivery much too high even in the control series.]

W. I. C. Morris

441. **Amnesia During Parturition. Use of Pentobarbital Sodium and Scopolamine Hydrobromide.** By P. P. VOLPITTO. *J. Amer. med. Ass.*, **132**, 1059–1062, Dec. 28, 1946. 1 fig., 17 refs.

The author reports on the use of pentobarbitone sodium (" nembutal ") and scopolamine hydro-bromide intravenously in 170 obstetric cases. The object was to obtain amnesia, not analgesia or anaesthesia. The contents of a pentobarbitone sodium ampoule (0.25 g.; 3¾ gr.) and a scopolamine hydrobromide ampoule (0.00064 g.; 1/100th gr.) are mixed and diluted to 10 ml. with sterile distilled water. Each ml. of this dilution thus contains 0.25 g. of pentobarbital sodium and 0.000064 g. of scopolamine hydrobromide. In normal primiparae or multiparae, as soon as regular pains develop—4 to 5 minutes apart and lasting 30 or more seconds—the combination is given intravenously. An initial 3 or 4 ml. of the mixed agents is given fairly rapidly at the rate of 1 ml. every 5 or 10 seconds; then the injection is slowed to the rate of about 1 ml. every 30 seconds, until the patient either begins to fall asleep or talks incoherently. At this point the injection is stopped, but the needle is kept in place and the patient is watched during a uterine contraction. If she is extremely restless during this pain and talks coherently an additional 1 to 3 ml. at the most is administered. On the other hand, if the patient is slightly restless or opens her eyes and talks incoherently no further injection is given. The average patient, whether primipara or multipara, will require a total initial injection of 10 ml. of the mixture. As little as 6 ml. and as much as 20 ml. has been found necessary in some cases. A patient whose cervix is fully dilated and who is beginning to bear down with each pain may require greater initial or additional amounts. However, extreme caution is necessary at this time as amnesia and not analgesia is sought; hence more restlessness should be expected at this time. Care must be taken not to mistake momentary lucid intervals, such as recognition by the patient or the request for the relief of pain, as indications for administration of more drugs. After the initial induction of amnesia the frequency and amounts of further injections will depend on the particular patient and the progress of labour. When the patient tends to become restless during the pain or does not sleep and is somewhat lucid between uterine contractions, the administration of more of the drugs is indicated. This will generally occur about three quarters to 1 hour after the first injection, and not more than 2 ml. of the diluted mixture will be required The average multipara, unless the cervix is fully dilated

at the start, will need yet another 2 ml., and the average primipara about three such injections. The interval grows longer with each injection—that is, 1 hour for the first, 2 hours for the second, and 3 to 4 hours for the third.

In the 170 women there were 75 primiparae and 95 multiparae; 96.4 per cent delivered spontaneously and 3.5 per cent required low forceps. Complete amnesia was reported by 89.4 per cent, and partial amnesia by 10.6 per cent. In 16.6 per cent there was an apparent slowing of either the first or the second stage and in 2.9 per cent, labour pains ceased completely after the administration of the drugs. Three patients (1.7 per cent) became extremely excited and almost unmanageable in the early second stage; 20 per cent became " exceedingly restless " during the latter part of the second stage. A severe drop in blood-pressure occurred in 2 patients and was associated in both with a too rapid injection; both quickly recovered on intravenous injection of 2 mg. of " neosynephrine " hydrochloride and administration of a high concentration of oxygen. Too rapid injection caused severe respiratory depression in 1 patient. Nausea and vomiting occurred in 3 patients. There was one maternal death; this patient had been given 15 ml. of the mixture in two injections and shortly after the second became cyanotic and dyspnoeic with a pulse rate of 160 and systolic and diastolic blood-pressure of 70 and 40 respectively; 2 hours later a stillborn foetus was delivered by high forceps. Of the infants, 92.4 breathed spontaneously immediately after birth and 7.6 were apnoeic, all but 1 being successfully resuscitated. The author concludes that the method is an efficient and safe one for obtaining satisfactory amnesia during labour.

F. J. Browne

442. The Use of Rectal Pentothal Sodium in Obstetrics.

By E. W. FERGURSON. *North Carolina med. J.,* **8**, 84–86, Feb. 1947. 9 refs.

Thirty obstetric cases are reviewed in which rectal pentothal, in conjunction with " demerol " (pethidine) and scopolamine intramuscularly, was employed for analgesia. While it is appreciated that no absolute conclusions can be drawn from this small series of cases, the paper is presented in the hope that it will stimulate further study on the use of rectal pentothal in obstetrics. The author has observed that the intramuscular administration of demerol in doses of 50 to 100 mg. and of scopolamine in doses of 1/200 gr. (0.32 mg.) during the first stage of labour greatly enhances the action of rectal pentothal. By combining the drugs he has found that a single dose of 1 g. per 65 pounds (30 kg.) of body weight is sufficient to maintain analgesia in practically every case, whereas the dose of pentothal previously recommended for prolonged analgesia was 1 g. per 50 pounds (23 kg.) body weight, followed about 1½ hours afterwards by a further 1 g.

The pentothal is administered by rubber catheter into the rectum when the cervix is dilated to about 3 cm. in multiparous patients and to 4 cm. in primiparae. The dose required is calculated on the patient's weight as recorded at the last prenatal visit. A sensation of drowsiness and tingling in the extremities usually follows within 2 to 5 minutes. Occasionally during the second stage of labour it may be necessary to give inhalations of nitrous oxide and oxygen to avoid administration of further pentothal. With the technique described complete analgesia and amnesia was obtained in all except 2 of the mothers in the series. These 2 were the first patients delivered in the clinic by this method, and neither demerol nor scopolamine had been employed. In practically every case the patient slept continuously. Drowsiness and relaxation frequently continued for from 2 to 8 hours. The author believes that the first stage of labour is shortened by the use of rectal pentothal and that there is no increased tendency to haemorrhage, relaxation of the uterus, or placental retention.

No maternal or foetal death was recorded. Three babies required cardiac or respiratory stimulation, but the author considers that in none of them was the difficulty attributable to the drug. Throughout the series no untoward maternal reactions to the drug were noted. Pentothal is contra-indicated in patients with respiratory or cardiac embarrassment. The drug may have a depressant effect on the respiratory centre of the foetus, and particular care must be exercised in cases of prematurity; similar caution is required in pre-eclampsia. " Nembutal ", " seconal ", and other barbiturates should not be used in conjunction with rectal pentothal.

R. L. Hartley.

443. **Sodium Pentothal Anesthesia in Major Obstetric and Gynecologic Surgery. Preliminary Report of 300 cases.**

By V. P. MAZZOLA. *Amer. J. Obstet. Gynec.,* 53, 207–213, Feb. 1947. 2 refs.

PUERPERIUM

444. **The Effect of the Anticoagulants on Postpartum Bleeding.**

By A. C. BARNES and H. K. ERVIN. *Surg. Gynec. Obstet.,* 83, 528–530, Oct. 1946. 1 fig., 7 refs.

The anticoagulants dicoumarol and heparin might be useful in the treatment of puerperal thrombophlebitis. But is their use likely to increase vaginal bleeding or to cause postpartum haemorrhage? To get more accurate information on this point the authors measured vaginal blood loss in patients receiving these two drugs in the early puerperium. Blood-loss studies beginning 1 hour postpartum and continuing during the patients' stay in hospital were made on 30 consecutive primiparous women who had had normal labours at term. All perineal pads were collected over the period the patient was in hospital; the pads of the preceding 24 hours were washed out daily in a measured volume of water and the haemoglobin measured in the wash water. Prothrombin levels and clotting times were determined for all these patients, 14 of whom were given dicoumarol and 5 heparin; 11 control patients received neither.

The dicoumarol was given in doses adequate to depress prothrombin levels to the therapeutic range—300 mg. during labour, 200 mg. on each of the first 2 days postpartum—while subsequent doses were adjusted by the prothrombin determinations. The drug was discontinued 24 to 48 hours before the patients left hospital. Graphs show the average daily prothrombin level and the average blood loss for patients receiving dicoumarol and for control patients. There was no significant difference in the average blood loss in the two series. Bleeding and clotting time in the nursing babies showed prolongation in one-third of the cases.

The action of heparin is more rapid, and the drug was used more cautiously to obtain a prolonged clotting time only for a 24-hour period on either the first or second day postpartum; considerable increase in the clotting time was observed, but no increased vaginal bleeding. Patients with thrombophlebitis were not treated, the study being undertaken to determine whether or not, should these drugs be indicated, increased vaginal bleeding prohibited their use. The series is small, but the data obtained showed that these two drugs are not necessarily contra-indicated in the puerperium.

Eardley Holland

445. **Puerperal Inversion of the Uterus.**

By R. TORPIN. *J. med. Ass. Georgia,* 36, 63–69, Feb. 1947. 6 refs.

446. **Complete Absence of Lochia Following Delivery. Report of a Case.**

By R. J. HEFFERNAN and C. L. SULLIVAN. *New Engl. J. Med.,* 236, 65–67, Jan. 9, 1947. 12 refs.

On account of toxaemia of pregnancy, breech presentation, and disproportion, an elderly primigravida was delivered by lower segment Caesarean section after pregnancy had lasted 36 weeks. No lochia at all was passed and on the twenty-first day after delivery the patient menstruated normally. Periods continued at 28-day intervals afterwards. The puerperium was apyrexial.

[It appears probable that in this case membranes obstructed the internal os. There is no mention of any step being taken, in the course of the operation, to find out whether the cervix was left patent.]

D. M. Stern

447. **An Outbreak of Puerperal Infection in a Maternity Home Caused by Sulphonamide-Resistant Streptococci.**

By A. A. MILLER and P. KIDD. *Mon. Bull. Min. Hlth.,* 5, 245–248, Nov. 1946. 1 ref.

The authors, working at the Emergency Public Health Laboratory, Reading, England, record an outbreak of puerperal fever in a small maternity hospital in which 8 out of 11 patients were involved. There had been puerperal pyrexia in some earlier cases in which it had not been customary to collect bacteriological specimens, but simply to administer sulphathiazole. In the outbreak recorded in the present paper, sulphathiazole was not as effective as previously, and so bacteriological investigations were carried out. Haemolytic streptococci were isolated from 8 vaginal swabs, and all belonged to Group A and Type 19. Further, when the sensitivity of the strains to sulphonamides was tested

all were found to be resistant to 1 mg. per 100 ml., and 6 out of the 8 to 5 mg. per 100 ml. of sulphanilamide and sulphathiazole. Some of the cases required penicillin to effect a cure. The home was closed for 2 weeks and thorough sterilization and disinfection were carried out, but when patients were readmitted there was a further infection. Throat and nose swabs from the staff were examined; one only showed haemolytic streptococci, but this did not belong to the same type as the strains isolated from the patients. The presumption was, therefore, that case-to-case infection had taken place. The lesson to be learnt from this outbreak is that, despite the undoubted value of sulphonamides, bacteriological examination is still necessary in cases of puerperal pyrexia, and the same measures of control should be adopted as in the pre-sulphonamide days.

J. Smith

448. **A Case of Puerperal Septicaemia due to Fusiformis Necrophorus.**

By T. V. COOPER and J. A. ROBSON. *Mon. Bull. Min. Hlth.*, 6, 10–12, Jan. 1947. 1 fig., 4 refs.

After a brief survey of the literature the authors describe a case of puerperal septicaemia due to the *Fusiformis* group of organisms. The description includes a case report with full temperature chart and a detailed account of laboratory investigations. Colonies of the organism appeared on the surface of sedimented blood after 72 hours' anaerobic incubation at 37°C. The organism was sensitive to penicillin *in vitro*. The patient responded quickly to penicillin treatment. Convalescence was uneventful and the patient was normal 5 months later.

R. H. Parry

449. **The Treatment of Acute Postpartum Thrombophlebitis of the Lower Extremity by Continuous Caudal Anesthesia.**

R. C. BENSON. *Amer. J. Obstet. Gynec.*, 52, 830–836, Nov., 1946. 14 refs.

Five cases of acute postpartum thrombophlebitis of the lower extremity (3 deep femoral and 2 superficial saphenous) were treated by continuous caudal analgesia. The method is based on the theory of Leriche and Kunlin (1934) that vasospasm is the important factor in the thrombophlebitic process and the practical application of this theory in the treatment of the condition by

sympathetic nerve block following paravertebral injections of local analgesics, a method popularized particularly by Oschner. The success of continuous caudal analgesia in relieving pain and spasm in obstetrics suggested that the same method might be effective in overcoming the pain and vasospasm in acute thrombophlebitis.

Thirty ml. of 1.5 per cent " metycaine " in Ringer's solution was injected into the sacral space through the sacral hiatus. Twenty ml. of the solution was injected (hourly for 4 hours or more) through the sacral needle which remained in position throughout the period of treatment, during which the patient lay on the side or back with the legs a little elevated. Pain was relieved in about 15 minutes, and was not likely to return during the course of 12 or more hours of treatment. Temperature returned to normal in 12 to 24 hours, oedema subsided in about 24 hours, and tenderness disappeared in about the same time. " Pontocaine " 0.15 per cent with 30 ml. as an initial dose, was used in some of the cases. The method is stated to be particularly applicable to acute cases; it is doubtful if it is likely to be beneficial in chronic cases.

T. C. Clare

450. **Acute Postpartum Necrosis of the Anterior Hypophysis.**

By E. W. NELSON and J. P. MICHAELS. *Amer. J. Obstet. Gynec.*, 52, 817–825, Nov. 1946. 2 figs., 16 refs.

A woman, aged 32, primigravida, was admitted in labour at 8½ months with generalized tonic and clonic convulsions; her blood-pressure was 207/160 mm. Hg. The onset of labour was spontaneous and delivery assisted by low forceps. Blood loss was moderate (400 ml.). The patient passed into a condition of shock immediately after the expulsion of the placenta and blood-pressure fell to 78/50 mm. Hg. Blood transfusion had no effect on the blood-pressure, which, however, rose to 90 to 100 mm. systolic after intravenous injections of adrenaline. Urinary output was very scanty during the next 24 hours, but there was slow improvement after large doses of intravenous hypertonic glucose. Because of anaemia she was given 500 ml. of citrated blood, followed in error by the infusion of a litre of distilled water. Twelve hours later the patient was

apparently moribund; however, there was dramatic improvement after the intravenous administration of 300 ml. of 5 per cent sodium bicarbonate followed by 50 ml. of 50 per cent glucose. This was given because of a clinical impression of hypoglycaemia. More glucose was administered to combat a relapse into a semi-comatose condition. It was noted that all this glucose failed to raise the blood-sugar level or to promote glycosuria.

The continued necessity for the use of 50 per cent glucose on account of coma led to the decision that this case was one of anterior pituitary necrosis. "Antuitrin" therapy was begun but no improve-ment was noted after 12 hours. The next day treatment was started with desoxycorticosterone acetate (DOCA) in conjunction with sodium chlo-ride administration, 20 mg. of DOCA being given in the first 24 hours with a maintenance dose of 15 mg. daily afterwards. Some improvement followed; but an attempt to reduce the dose of DOCA was followed by a relapse into coma, with mild con-vulsions. On the 15th day the patient was allowed to get up in a chair, but two days later thrombophlebitis developed in the right saphenous vein. The saphenous and femoral veins on that side were ligated and lumbar sympathetic block was performed. A general septic condition gradu-ally supervened and the patient died a month after the delivery. At necropsy, the pituitary weighed 0.506 g. In the anterior lobe 85 per cent of the gland substance was occupied by a yellow depressed area and the entire anterior lobe stained pink with-out any cellular details. The posterior lobe was normal.

[A point of particular interest about this case is that the diagnosis of anterior lobe necrosis was made within a few days of delivery, not from symptoms described by Simmonds as character-istic, for these symptoms did not develop till a later period, but from "a clinical impression" of hypoglycaemia. There is at present no specific treatment of the condition in the acute stage, though the line of treatment followed here—namely, by hypertonic glucose and DOCA (to stimulate glucogenesis)—might have proved suc-cessful if it had not been for the thrombophlebitis, presumably started by the very concentrated glucose injections).   *T. C. Clare*

451. Treatment of Breast Abscesses with Penicillin. By M. E. FLOREY, J. S. MACVINE, and M. A. M. BIGBY. *Brit. med J.*, 2, 845–848, Dec. 7, 1946. 2 figs., 18 refs.

The authors have taken considerable trouble and time over this investigation of 34 cases.

TABLE I.
Comparison of Results in Breast Abscesses

	No. of Cases	Duration in Days after First Treatment of					
		Pyrexia		Suppuration		Healing Time	
		Mean ± S.E.	S.D.	Mean ± S.E.	S.D.	Mean ± S.E.	S.D.
Controls	16	7.5 ± 1.97	± 7.86	13.8 ± 3.0	± 12.0	26.5 ± 2.45	± 10.17
Treated	18	3.9 ± 0.91	± 3.73	6.3 ± 0.82	± 3.5	13.5 ± 1.50	6.37
Differ-ence		3.6 ± 2.17		7.5 ± 3.11		13.0 ± 2.87	

S.E. = Standard error of mean.   S.D. = Standard deviation.

The 16 controls were treated by one or two courses of 20 to 30 g. of either sulphathiazole or sulphamezathine; the abscesses were drained surgically, and the wounds were dressed or irri-gated with eusol and subsequently treated with acriflavine and lotio rubra. A course of 30 to 65 mg. of stilboestrol was given over a period of three to five days. In 18 cases treated with penicillin, stilboestrol was given to only three patients. The decision to administer penicillin depended upon the state of the breast when first seen. In 13 cases *systemic penicillin* was given by the intramuscular route in a dosage of 15,000 units 3-hourly for a duration of 12 hours as a minimum and 3½ days as a maximum.

Aspiration and injection of penicillin under local analgesia once in 24 hours was performed in 10 abscesses as soon as fluctuation could be detected. A West Middlesex needle and stylet were used, and the puncture was performed through intact firm skin. All pus was evacuated and 120,000 units of penicillin in saline, equivalent to two-thirds of the volume of pus removed, were injected into the cavity if the inflammation was not fully localized; if it was localized 500 units per ml. were injected into the cavity, the puncture being sealed with collodion. If there was more than one abscess each was given similar treatment. The abscesses so treated contained not more than 10 ml. of pus and required daily aspiration and injection for 4

to 7 days. *Instillation of penicillin after expression of pus* was performed on 5 abscesses. Spontaneous discharge of pus under systemic administration of penicillin was treated by the expression of pus every 24 hours and instillation along the sinus of penicillin through a suitable catheter or needle, the sinus being closed by collodion. A combination of the two methods of local treatment was employed in 5 abscesses, a needle being left in the abscess cavity and instillation performed through it. Sinuses developed along this tract in a day or two, and this added a week to the healing time, but the authors noted that the patient's comfort was very much greater. *Instillation following incision and suture* was performed on 4 abscesses. These were abscess cavities containing 100 ml. or more. The abscesses were drained through intact firm skin and a rubber tube was snugly sutured in position. Pus was expressed through this tube and instillation performed through it twice a day for 4 to 8 days. The authors again noted that this was a very comfortable method for the patient, and patients preferred instillation to intramuscular injection or aspiration and injection. They state that little work on penicillin in breast abscesses has. been reported, and reiterate that the social problems of this malady are considerable. They consider that now that penicillin is freely available large systemic doses and surgical incision might eliminate sepsis as rapidly as the employment of small doses of penicillin systematically and local instillation. They emphasize that if local instillation is used a rigid technique and experience are necessary.

TABLE II.

	Control	Treated
Total number of days spent in hospital	348	191
Total period of out-patient treatment	313	41
Total	661	232

In the penicillin series the healing time was half that of the controls, and suppuration was hastened rather than retarded [with the dose of penicillin employed] but subsided more rapidly. Stilboestrol was unnecessary and the mother continued suckling throughout treatment. The number of operations [general anaesthetics] was reduced from 22 to 4. [The number of surgical procedures with or without local analgesia appeared to be many, however.] The total number of days of treatment was reduced from 661 to 232.

[In respect of healing time the authors have shown again that penicillin is the chemotherapeutic agent of choice in the treatment of breast abscesses. Is it not time that sulphonamides should be abandoned in this type of case Unfortunately in the past a recurrence of the disease some time later has not been uncommon. A follow-up of 1 to 6 weeks is not an absolute indication that these cases will not recur. This penicillin investigation has been very valuable, but the authors' technique and dosage will not necessarily be accepted as the method of choice. Systemic penicillin is essential to abort the early case or to localize the abscess; Taylor and Way (*Brit. med. J.*, 1946, 2, 731) have recently emphasized this point. Other workers have found that a dose of 60,000 units 3-hourly is infinitely superior to one of 15,000. Many patients are intolerant of, and find extremely painful, aspiration and injection under local analgesia, The authors themselves comment on the fact that patients whose abscesses had undergone spontaneous rupture or were afforded reasonable drainage were much more comfortable. Breast abscesses are a social calamity, and it is probable that lack of space in periodicals has prevented other workers from publishing their results. In March 1946, in a progress report to the Medical Research Council, the Middlesex Hospital staff stated that after a trial of various methods a dose of 60,000 units 3-hourly and temporary drainage of an abscess—if it formed—by means of a ¼-inch (0.6 cm.) incision gave the best results. A follow-up of one year showed no recurrence.]

R. Vaughan Hudson

THE INFANT.

452. Intracranial Damage in the Newly Born.
By T. Y. NELSON. *Med. J. Austral.*, **1**, 268–270, Mar. 1, 1947. 7 refs.

The author deals with the clinical diagnosis of established cases of intracranial haemorrhage, with special reference to active treatment. The particular group considered is that in which the damage

is apparently great and the symptoms so severe that survival of the infant is in doubt. Haemorrhage into the subdural space constitutes the largest group, as well as the most important one as regards the probability of successful treatment, whether to save life or to prevent disabling sequelae. Tentative diagnosis may be confirmed by needling through the coronal suture lateral to the fontanelle. Improvement often follows the withdrawal of even a small amount of blood. Gradual decompression by the withdrawal of small quantities daily is recommended. In some cases, after 2 or 3 weeks, a burr hole may be made in the temporal region for the withdrawal of more blood or for exploration.

Over a period the author has examined a number of infants with a tentative diagnosis of this lesion, and the presence of haemorrhage has been established in 6. Of these 4 developed normally after active treatment and 2 were left with spasticity and mental defects. The series is a small one but, as the author states, it is presented in the hope that further interest may be stimulated in an important and difficult subject.

Eardley Holland

453. Bilateral Harelip and Unilateral Harelip with Cleft Palate in Fraternal Twins.
By P. A. SHEA and R. B. NELSON. *Amer. J. Obstet. Gynec.*, 53, 340, Feb. 1947. 1 ref.

454. Sympus Apus. A Case Report.
By L. H. BISKIND and A. M. YOUNG. *West. J. Surg.*, 55, 94–96, Feb. 1947. 4 figs., 2 refs.

455. Final Observations on Congenital Defects in infants following infectious Diseases during Pregnancy, with Special Reference to Rubella.
By C. SWAN, A. L. TOSTEVIN, and G. H. B. BLACK. *Med. J. Austral.*, 2, 889–908, Dec. 28, 1946. 32 refs.

This paper records the results of a second study of 2 earlier series of cases of congenital defect in infants subsequent to maternal rubella in pregnancy and of the study of a fourth series of cases, and summarizes the results of the South Australian investigations carried out during the last 5 years. A table gives an analysis of the data obtained on re-examination of 61 children whose mothers had suffered from rubella in pregnancy. Details of the congenital defects present and of the physical development of these children are shown. Another table gives an analysis of type and period of onset of infectious disease during pregnancy and of the congenital defects in 25 infants born subsequently. The summary is based on the present and earlier papers. This records the congenital abnormalities found following rubella, morbilli, mumps, variecella, herpes zoster, scarlet fever, and influenza during pregnancy. Out of 154 infants whose mothers suffered from one or more of the above-mentioned diseases, 119 showed congenital malformations. In 3 further cases, congenital malformations occurred in the offspring in the absence of a history of maternal infection during pregnancy. These findings are discussed in detail. In this series only 3 out of 62 babies whose mothers had had rubella in the first 2 months of pregnancy were free from congenital abnormalities. Thus it is possible that rubella in early pregnancy is not invariably followed by congenital defects in the baby. Fox and Bortin have reported on an epidemic of rubella in Milwaukee during 1942–44. Eleven women suffered from the disease in the first 4 months of pregnancy. One mother was delivered of a stillborn hydrocephalic infant, and with one doubtful exception, in all of the remaining instances the babies born subsequently were normal. These diametrically opposed American findings may have been due to an error in diagnosis or to an alteration in virulence of the virus. No conclusive evidence is yet available with regard to the effect on the foetus of other infectious diseases during pregnancy.

J. M. Smellie

456. Treatment of Premature Infants with Quinton's Serum. (Sul trattamento dei prematuri con il plasma di Quinton. Studio di osservazioni cliniche di prematuri presso la clinica ostetrica di Ginevra.)
By G. PIANO. *Ginecologia*, 12, 218–230, July–Aug. 1946. 6 figs., 16 refs.

In 1907 Quinton introduced his " serum " into postnatal therapy. Between 1938 and 1944 about 1,000 premature and debilitated infants were treated with this serum in the Geneva maternity hospital. The results obtained are described in this article. Quinton himself defines the preparation as " sea water of absolute purity, approximately isotonic to human plasma, sterilized without the use of boiling or of chemical agents, and

stored in sterile glass containers ''. One can prepare a practically isotonic solution by adding 5 parts of distilled water to 2 parts of sea· water. In sterilization the method of choice is cold filtration, as sterilization by heat has numerous disadvantages. Some preparations are on the market under proprietary names. There are relations between the composition of sea water and that of the '' vital milieu '' of organisms; in the case of the vertebrates the blood plasma. Chemical elements are found in both in approximately the same percentage.

Parenteral administration of the sea water is to be preferred to oral use. The doses vary, according to weight and age of the patient, from 10 to 60 ml. The author gave subcutaneous injections of not more than 20 ml. a day. The serum should be warmed to body temperature. Properly prepared sea water has no toxic effects; it is possible to inject into dogs an amount of sea water equalling 60 per cent of their weight without any ill effects. The beneficial action of Quinton's serum is explained by increase of blood volume, acceleration of circulation, and increase of renal function. In addition to these physical factors the minerals have an important chemical function in the metabolism of the cells, tissues, and the whole organism. The foetus, particularly in the last months of its intrauterine life, selects those minerals which are of vital importance to its development. This explains the therapeutic value of the serum for infants who—owing to their prematurity (more correctly, immaturity)—suffer from a mineral deficiency.

For the evaluation of the clinical observations infants were classed as debilitated when signs of prematurity were missing, the weight was below 2,500 g., and the length below 50 cm. Infants with signs of prematurity were divided into three classes : (a) length at birth 40 to 44 cm.; (b) length at birth 44 to 46 cm.; (c) length at birth 46 to 48 cm. As most infants did not remain more than 10 days in hospital, the condition and weight of the infant on the tenth day were compared with those factors at birth. The results of the observations are as follows : 22.84 per cent had recovered their birth weight, 42.61 per cent had passed it, 32.82 per cent had not yet reached it, and 1.72 per cent had died. Two of these 9 infants died of cerebral haemorrhage. It should be pointed out

that the hospital is not provided with incubators. In the normal infant the birth weight is usually regained between the eighth and twelfth days, but in the premature infant recovery of the birth weight is usually only achieved after weeks. In addition to these two curves the author adds the weight curves of the premature infants treated with serum, separate curves being given for classes (a), (b), and (c). Their course differs from that in the untreated premature infant and approaches that of the full-term baby. The descending phase is diminished, the rise earlier and regular. A sixth graph shows the curves of the normal and, the premature infant, and the mean of curves (a), (b), and (c), all originating from a point which represents the weight at birth. From this it is obvious that the loss of weight in premature infants · treated with serum is relatively even less than that of normal infants and that the birth weight is regained on the tenth day. The author believes that the addition of Quinton's serum to the usual therapeutic measures will improve the prognosis of prematurity.

Hilde Eisner.

457. Measures for the Protection of Newborn Infants. I. Description of Measures Instituted in May 1937, at Long Island College Hospital.
By C. A. WEYMULLER, A. C. BECK, and E. J. ITTNER. *J. Amer. med. Ass.,* 133, 78–84, Jan. 11, 1947. 11 figs., 2 refs.

The authors discuss measures employed since May, 1937, to control cross-infection among infants in the Maternity Unit of the Long Island College Hospital, Brooklyn, where 1,500 infants are cared for annually. Among circumstances favouring infection in nursery units are, unnecessary visiting, especially by children; overcrowding of infants in nurseries; assignment of nurses to duties which entail contact with a large number of infants; proximity of milk-room to nurseries, and return of unsterilized implements from nurseries to milk-room; proximity of isolation to uncontaminated units. Arrangements in the Brooklyn unit were designed to avoid these and other dangers.

Reduction of contacts was achieved as follows : (a) Visiting times to mothers were only 5 hours per week. Visitors wear masks and gowns and are separated from beds by rope barriers. (b) Throat cultures are made from nurses before duties are

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begun; rejection occurs if possible pathogens are found. Masks and gowns are worn constantly in nurseries. (*c*) The physician enters the nursery only in emergency, and normally works in an examination room attached to each nursery unit (Fig. 1). Gown, mask, and gloves are worn, and are changed on moving to another nursery unit. House officers are confined to duties in a single unit. (*d*) Ward maids observe similar restrictions.

Drugs and diagnostic apparatus are duplicated in each nursery unit. Sterilized bedding and clothing are supplied daily to each nursery and placed beside individual beds. The layout of the nursery unit is carefully designed (Fig. 1). Although units are for 16 cribs, an 8 crib unit is considered better

FIG. 1.

FIG. 2.

by the authors. Prevention of case to case contact by intermediaries is practised as follows: (*a*) One nurse cares wholly and solely for a group of 8 full-term babies and 1 premature baby. (*b*) The layout of the milk-room is shown in Fig. 2. It is distant from the nurseries. All material enters through a sterilizer in an anteroom. Sterile precautions are observed by nurses working in the milk-room; nurses are withdrawn if they develop any infection. Milk mixtures are pasteurized (140° to 160°F. (60° to 71°C.) for 30 minutes) after preparation. Before return to the milk-room utensils are sterilized in the nursery. Sterile milk mixtures are taken to the refrigerator in each nursery unit in a closed cart. The " utility room " commonly attached to nurseries is eliminated. (*c*) An isolation unit, distant from the nurseries, is provided for infants suspected of infection, and sick infants are rigidly isolated in the separate paediatric section.

Skin infections are reduced by routine prophylactic anointing of each infant soon after birth with 15 g. of 5 per cent sulphathiazole ointment, repeated if any contact occurs with infection. By this measure the incidence of pyodermia was reduced to 0.9 per cent from a previous level of 16 per cent. If an infection develops in a nursery unit, the affected infant is isolated and the contaminated unit is closed to all admission until risk of further infection is over, and when empty is scrubbed with soap and water, no admission being permitted for a full 24 hours thereafter.

The good results ensuing from this prophylactic technique are considered, and the methods of control of an epidemic of diarrhoea which followed a breakdown of the technique due to wartime shortage of nurses are described. During the epidemic it was established that if the technique outlined above is followed closely (*a*) a common milk-room for all infants, sick or well, can be used without risk of cross-infection, and (*b*) a clean nursery can, without cross-infection, be operated beside one contaminated with neonatal diarrhoea.

                                                    M. MacGregor

458. **Epidemic Diarrhea in the Newborn.** The relation between Breast and Bottle Feeding and the Early Development of the Proper Intestinal Flora. By H. W. MAYES. *Amer J. Obstet. Gynec.*, **53**, 285–289, Feb. 1947. 3 refs.
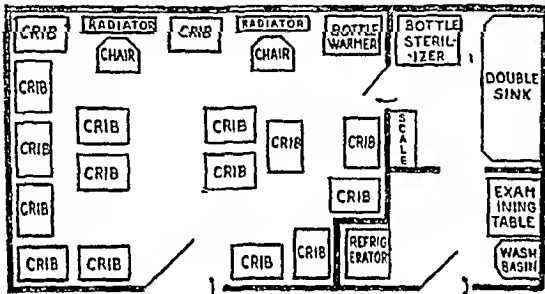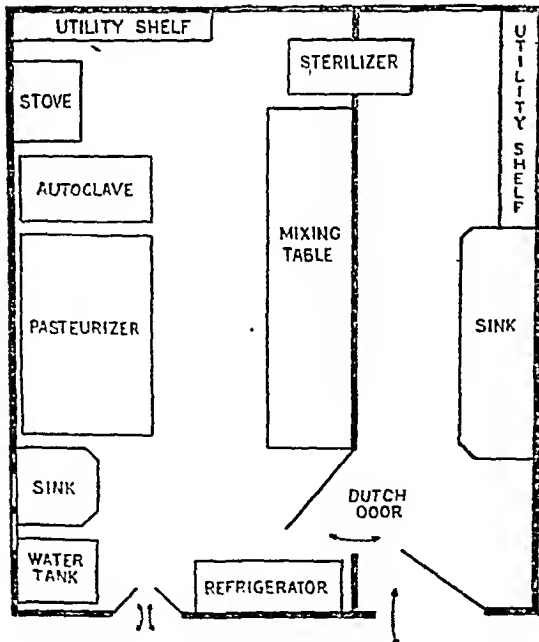
459. Bacteriology of the Oronasal Cavity of the Newborn.

By J. L. CORNELISON, E. A. JOHNSON, and W. M. FISHER. *Amer. J. Obstet. Gynec.*, 52, 797–802, Nov., 1946. 6 refs.

Two groups of new-born babies were studied. In the first group, consisting of 100 unselected new-born infants, an attempt was made by the use of selective media to isolate staphylococci, coliform bacilli, and moniliae from the oronasal pharynx and nasal orifices. The second group of 50 unselected new-born infants was studied with special reference to streptococci and pneumococci. The bacteriological results were correlated with the type of delivery and length of time of rupture of the membranes.

There were no staphylococci, coliform bacilli, or moniliae in 39 of the 100 cultures in the first series; 21 plates were positive for coliform organisms, and of these 11 showed the cultural characteristics of *Bacterium coli*. Yeast strains were isolated in 11 cases but only 2 were *Candida albicans*. Forty-four strains of haemolytic staphylococci were isolated, 2 of which were coagulase-positive. The longer the membranes were ruptured before delivery the higher was the percentage of positive cultures. Positive cultures for staphylococci, coliform bacilli, or moniliae were obtained in 64 per cent of the infants delivered spontaneously and in 61 per cent of those delivered by low forceps. Two infants delivered by mid-cavity forceps gave positive cultures for staphylococci, but 2 delivered by Caesarean section were negative for the three organisms studied.

Pneumococci were not found by the methods used in the second group of unselected new-born infants, but α-streptococci were found in 6 cases and β-streptococci in 4. The fact that both strains of streptococci grew at 45°C. and were not killed by heating for 30 minutes at 60°C. indicated that they belonged to the enterococcus group. There was a larger percentage of β-streptococci present when the membranes had been ruptured a long time or when forceps had been used.

T. N. MacGregor

460. The Problem of the Suckling. (Zum Stillproblem.)

By W. R. MERZ. *Schweiz. med. Wschr.*, 76, 1177–1179, Nov. 16, 1946. 2 figs., 24 refs.

Statistics for breast feeding in Switzerland are presented. During the last 20 years the rate has remained stationary and unsatisfactory in spite of continuous propaganda and the award of certain benefits to mothers who breast-feed their infants. At the end of the tenth week the rate was approximately 55 per cent. The negative attitude of the mothers and the relative inactivity of the maternity hospitals in combating this attitude, probably due to lack of well-trained nursing staff, are regarded as the principal causes of this position. A table compares the breast-feeding rate at the time the mother is discharged at several Swiss hospitals for a period of 11 years (1934–44). The figures vary considerably (from 46.4 to 83.5 per cent). The suckling ability of 2,400 healthy mothers with healthy babies was checked during the first 10 days after birth, the decisive period for the initiation of breast feeding. Three groups are distinguished: total breast feeding, partial breast feeding, and artificial feeding. In the first group all mothers were included who could satisfy the individual requirements of the infant. The mutual relations of these groups are charted. The typical increase of the breast-feeding incidence during the first 3 to 4 days and the sudden decline on the sixth and seventh days are demonstrated and the principal causes explained. On discharge only about 50 per cent of the mothers (54 per cent on the ninth and 52 per cent on the 10th day) were wholly breast feeding, an unsatisfactory rate. The problem of hormonal relationship between the mother's suckling ability and the engorgement of the breasts in the new-born was studied in 450 cases. The group of mothers who were partially breast feeding on the ninth or tenth day (41 per cent) was subdivided according to degree of suckling ability. The result was inconclusive. No correlation between the incidence and degree of engorgement, and suckling ability could be found.

A short survey of measures, old and new, for promoting the ability to breast feed includes general rules for the pregnant woman, for drug treatment, for the care of the breasts during the onset of lactation, and for the prevention of complications during labour and the puerperium. Incidentally, mastitis has the least influence of all complications on the suckling ability. The maxim is accepted that "a bad conduct of breast

feeding has a greater bearing on infant mortality than a bad conduct of labour."

[The figures for England and Wales for the years 1931–41 indicate a decline in initial incidence of breast feeding of 5.6 per cent. About 80 per cent of the babies leave the hospital wholly breast fed. At the end of the third month the rate is 50 per per cent.   The most effective measures to promote breast feeding are the utmost restraint in the introduction of complementary feeding, complete emptying of the breasts after each feed, and adequate nutrition of the mother. Thus a breast-feeding rate of 98 to 99 per cent can be achieved.]

M. Dynski-Klein

461. **Causes of Stillbirth.** (Neonatale sterte en haar oorzaken.)
By F. WILLEMIJNS. *Belg. Tijdschr. Geneesk.*, **3**, 301–316, Apr. 1947. 3 figs.

462. **Studies in Infant Mortality. Part II. Social Aetiology of Stillbirths and Infant Deaths in County Boroughs of England and Wales.**
By B. WOOLF. *Brit. J. soc. Med.*, **1**, 73–125, April 1947. 6 figs., 17 refs.

This is a very important contribution to our knowledge of the aetiology of stillbirths and infant deaths; it is a sequel to a previous paper by Woolf and Waterhouse (*J. Hyg. Camb.*, 1945, **44**, 67).   The earlier article contained statistical tests showing the social and medical reasons for regarding the relation between infant mortality and the social variables as a real one, in the sense that improvements in social conditions might be expected to reduce infant deaths. But it did not deal with the questions of social aetiology; of how overcrowding, low earnings, and so on exert their influence on the life of the baby. This further aetiological analysis, however, is carried out in the present paper and regression equations are given for the separate diagnostic groups and age periods during which death occurs. It also deals with stillbirths.

In the first paper, for the 11 years 1928–38 inclusive, the average equation was $M = 23.1 + 0.51H + 0.46U + 0.29P + 0.35F + 2.01L$, where the indices used were:

H = Percentage of families with more than 1 person per room.

U = Average monthly percentage unemployment amongst adult males.

P = percentage of occupied males in social classes IV (semi-skilled) and V (unskilled) workers).

F = Percentage of females aged 14 years and over employed in manufacture.

L = Degree of latitude north of 50° 30′.

In the present paper an index expressing size of family (G) and one expressing local density of population (D) have been added. A regression constant (K) is also used to denote an estimate of infant mortality rate if adverse social conditions are excluded. The author deals with infant mortalities as a whole for different social grades according to individual cause and for different administrative areas. Congenital causes showed little variation according to social grading. Class V being to Class I in the ratio 1.5 to 1; but for pneumonia and bronchitis the ratio of Class V to Class I was 6.75 to 1, for infectious diseases 5.4 to 1, and for diarrhoea 4 to 1. Regarding areas, county boroughs had a total infant mortality rate of 70.8—12 units higher than for urban districts and London and 16 higher than for rural districts. Among individual diseases, London had a higher diarrhoea rate than county boroughs, but London had by far the lowest figure for congenital defects. Woolf deals largely with the rates for county boroughs, and in a table the regression equations are given for 82 of them for the 11 years 1928–38. Another table shows how infant mortality and still-birth-rates are associated with various social conditions; the different grouped causes of infant mortality; and the period in the year of a child's life in which death occurred.

Mortality rates associated with social indices grouped into aetiological categories are also tabulated.

The aetiological conclusions that would seem to follow from these figures are stated and discussed. They include the following: (a) Poverty (probably mainly malnutrition) and crowding are of approximately equal importance in infant mortality. Crowding is relatively unimportant in stillbirth rates, whereas poverty has a very big effect. For the combined rate, therefore, poverty is much the more influential, making an estimated contribution of about 37 as against 10.5 attributable to crowding. (b) At equal degrees of crowding and poverty, stillbirth and neonatal-death rates de-

crease with increasing size of family. This is in line with the fact that first births are known to carry an excess risk in these categories of mortality. In postnatal deaths and in all the zymotic-cause groups, larger families involve higher rates, because of the increased risk of infection of the baby by its elder sibs. (c) For the infectious diseases, bronchitis, and pneumonia groups, mortality increases with increased crowding (exposure to infection) and poverty (lessening of resistance). In diarrhoea, mortality increases with crowding, but at equal degrees of crowding seems to be greater for the better-off than for the poor. This is in line with the high diarrhoea rate in London. (d) Stillbirths and neonatal mortality tend to be lower in more densely populated and larger conurbations than in smaller communities. This is also in line with the comparative figures for London, and is attributed to the better social and medical care available in the larger places. (e) The disparity between well-off and poor is much greater in postnatal death rates, in which bad social conditions and large family size both act to increase mortality, than in stillbirths and neonatal deaths, where poverty and large family size act in opposite directions. (f) The effect of latitude is so distributed that it appears to be an expression of influences acting on the child at birth through the mother. (g) Industrial employment of women seems to be associated with increases in all categories of mortality. (h) The larger the family size the higher the mortality rate among live-born infants. But large family size decreases the still-birth rate so much that it more than cancels the increase in infant mortality. If the reproductive rate could be increased, other social conditions being unchanged, then a decrease would be expected rather than an increase in the rate of wastage of infant life.

The fall in stillbirth and infant mortality rates from the 1938 level during the war period is of the order of magnitude to be expected from the levelling up of nutritional standards among the worst-off section of the population. The estimated mortality rate (infant mortality plus stillbirths) in the " crowded poor " section of the population of county boroughs is computed as about 136, and of the " unemployed crowded poor " as about 232. The latter figure is more than twice the mean rate. Detailed comparisons are given between com-

puted rates at these social levels and that of the " better-off " section of the community. The scope and limitations of the multiple regression method are discussed, and the need for field research is emphasized.

E. H. M. Milligan

Rh factor, erythroblastosis foetalis.

463. **Review of Cases of Rh Iso-immunization during the Past Five Years in the Royal Victoria Montreal Maternity Hospital.**
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This paper reviews a total of 12,114 obstetric cases delivered in the 5-year period ending Dec. 31, 1945. There were 30 cases of haemolytic disease of the newborn—that is, 1 in every 404 deliveries. Of the 30 infants, 19 were born alive but 6 died before leaving hospital. Eleven of the remaining 13 have been followed up, and of these 8 are normal, and 3 are mentally retarded and have residual spasticity. Seven of the 30 pregnancies were interrupted at the thirty-sixth week, 5 by Caesarean section and 2 by other methods. This resulted in 4 live births and 3 stillbirths; only 1 of the 4 live infants survived. From the full-time pregnancies there were 15 live births and 8 stillbirths. Thus premature interruption did not yield good results. Among the 30 cases there were 4 of toxaemia, an incidence that is not significantly higher than that found in pregnancies not productive of haemolytic disease. Nor was there any case of retroplacental haemorrhage, which has been claimed to be more frequent in cases of Rh iso-immunization.

In the Royal Victorial Hospital, Montreal, all obstetric patients are tested for the Rh factor. If the patient is Rh-negative, her husband's type is determined. If this seems indicated, Rh-negative women are tested for antibodies at the third, sixth, and eighth month. If antibodies are present the type and titre are determined, and the titration is repeated each month. When the antibody titre increases to 1 in 100 this is taken as an indication of the foetal involvement, especially if the history denotes previous foetal mishaps. In 7 cases pregnancy was terminated at the thirty-sixth week for the purpose of lessening the damage to the foetus. If the husband is heterozygous and

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the history shows repeated foetal mishaps, contraceptives are indicated or even ligation of the tubes.

Early diagnosis is essential in the adequate treatment of the affected baby. The infants of all Rh-negative mothers, whether the latter exhibited antepartum antibodies or not, are typed for the Rh factor immediately after delivery. In this group daily haemoglobin estimations are done on all Rh-positive babies during their stay in hospital. If the haemoglobin is below 90 per cent at birth or if the daily fall is more than normal, repeated small transfusions are given (10 ml. per lb.: 22 ml. per kilo) of Rh-negative blood. Mothers' milk is not given, as it has been shown to contain Rh antibodies.

<div align="right">F. J. Browne</div>

464. *The Antepartum Prediction of Hemolytic Disease of the Newborn.*
By E. W. Page, M. Hunt, and S. P. Lucia. *Amer. J. Obstet. Gynec.,* 52, 794–796, Nov. 1946. 1 ref.

As the obstetrician is unable to forecast the outcome of the pregnancy in an Rh-negative mother, the present study was undertaken in the hope of formulating some guiding principle. The material for the study was selected from 4,000 pregnant women seen in the obstetric clinic of the University of California Hospital and in the private practices of six obstetricians. The blood serum of each patient was tested for agglutinating antibodies against two Rh-negative, group O, and two Rh-positive, group O, red blood corpuscle suspensions. Wiener's method was used for the detection of blocking antibodies.

It was apparent from a study of 26 cases, in which the time of appearance of the antibodies could be fixed, that when the antepartum duration of antibodies was 10 weeks or less erythroblastosis did not occur. Forty-nine cases were analyzed in which antibodies were detected in the blood more than 11 weeks before delivery. In 19 of these, traces only of either agglutinating or blocking antibodies were found. One case in this group developed a possible erythroblastosis foetalis—the child had a slight increase in nucleated red cells associated with a mild anaemia at birth. Appreciable amounts of antibodies or small amounts on repeated occasions were found in 30 cases. In 22 of these, antibodies

appeared more than 10 weeks before delivery and in this group there were 16 cases of erythroblastosis foetalis; the remaining 6 women were delivered of healthy infants, 4 of whom were Rh-negative. Further analysis of the figures showed that all the mild cases of erythroblastosis foetalis occurred in the 10 to 14-week group, while all the severe cases, including 7 of fatal hydrops foetalis, were in the group in which maternal antibodies had appeared at least 15 weeks or more before delivery.

The suggestions the authors make from this preliminary study are : (1) All pregnant women should be routinely typed and in all Rh-negative patients with Rh-positive husbands the blood should be examined for antibodies not later than the twenty-fourth week of gestation. (2) If the blood is strongly positive for either agglutinating or blocking antibodies, nothing need be done, as an Rh-positive foetus will be too seriously affected, while an Rh-negative foetus will escape the disease. (3) If antibodies are present only in traces or the presence of a small amount is not confirmed, the foetus is probably unaffected and it is unwise to interfere. (4) If no antibodies are found initially but a significant amount appears later, 8 to 10 weeks may be allowed to elapse before haemolytic disease becomes probable. Labour may be induced after this time provided it is within 6 weeks of term.

<div align="right">T. N. MacGregor</div>

465. **Kernicterus in Erythroblastosis Foetalis.**
By V. C. Vaughan. *J. Pediat.,* 29, 462–473, Oct. 1946. 27 refs.

Seventy-four cases of erythroblastosis foetalis have been diagnosed at the New Haven Hospital, Connecticut, in 17 years. There have been 27 deaths and 23 necropsies have been performed. A clinical account is given of the signs and symptoms preceding the death in 13 of the fatal cases, all of which were found at necropsy to have kernicterus. The specificity of opisthotonos and rigidity as signs of kernicterus was suggested by the fact that 4 survivors who showed these symptoms were mentally retarded and had some motor disability. The author finds a relationship between the occurrence of kernicterus and the severity of blood destruction, as measured by blood counts, by size of spleen, or by depth of jaundice. The time of

onset of icterus seemed to have no prognostic significance in this series. Kernicterus was found somewhat more commonly in the smaller babies, but the author claims no statistical significance for this observation.

The relation of transfusion to prognosis in erythroblastosis is considered. " It is seen that no infant who received Rh-positive blood on the first day of life died with kernicterus. This suggested superiority of Rh-positive blood . . . in preventing kernicterus is by no means statistically significant, but it represents the most striking deviation from the general finding that the type of blood used in therapy had no affect on the outcome." A discussion follows on the possible mechanism of production of the lesions of kernicterus. Early investigators of the Rh factor were unable to demonstrate it in cells other than the red blood cells. It now seems probable that the Rh factor is a general characteristic of tissue cells. But whether kernicterus represents a primary nerve-cell injury or primarily a vascular injury is still unknown. The possible role of " blocking antibody " in moderating blood-cell destruction is discussed, as is the use of Rh-positive blood transfusion to "mop up " circulating antibody. *A Doyne-Bell*

466. **Hemolytic Disease of the Newborn (Erythroblastosis fetalis). Treatment by a Single Massive Transfusion, with Complete Recovery.**
By A. BLOXSOM. *Amer. J. Dis. Child.*, 72, 320–324, Sept., 1946. 10 refs.

An infant with icterus gravis neonatorum was given a transfusion with 90 ml. Rh-negative blood and 50 ml. of plasma during the few hours following birth. The next morning it was given a further transfusion and, owing to an accident, received 310 ml. of blood in a short space of time. The infant became red and perspired freely but showed no other untoward effects. Whereas before the transfusion the infant's " reaction for the Rh factor " was only weakly positive, 10 days later it had become strongly positive. The author concludes that the transfusion supplied some " undoubted anti-antigen-antibody factor."

[There is no need to postulate any unknown factor to explain weakly positive Rh reactions in infants with icterus gravis. It has been shown that the red cells of such infants are coated with anti-

Rh antibody which sometimes makes them difficult to agglutinate. In time the supply of antibody is used up and the red cells then agglutinate more strongly.]
P. L. Mollison

OBSTETRIC OPERATIONS

467. **The Place of Caesarean Section in Modern Obstetrics.**
By J. BARNES. *Postgrad. med. J.*, 23, 157–161, Mar. 1947. 4 refs.

468. **Cesarean Section.**
By A. W. ANDISON. *Canad. med. Ass. J.*, 56, 170–177, Feb. 1947.

469. **Sulfonamides as a Prophylactic Agent in Conjunction with Cesarean Section.**
By H. C. HESSELTINE and C. THELEN. *Amer. J. Obstet. Gynec.*, 52, 813–816, Nov. 1946. 4 refs.

The authors state that from their observations " it is evident that the use of sulfonamide locally did not lower the morbidity rate or shorten convalescence. Furthermore, the bladder peritoneum seemed more adherent in a few patients subjected to laparotomy subsequently. This may not be serious, but it requires greater caution in the reflection of this tissue in subsequent laparotrachelotomies. Therefore, the local deposition of sulfonamides, either within the uterine cavity or over the uterine incision (but under the peritoneal reflection) did not reveal any prophylactic value. It did increase adhesions of the peritoneum to the uterus. There exist also the dangers of drug sensitization.

" The sulfonamides in relation to Cesarean section should be used on direct indication in relation to a proper bacteriologic study of the uterine cavity and blood stream, except in such urgent situations where the withholding of the drug would jeopardize the patient's convalescence or life. Even in this event, to-day penicillin would seem preferable to the sulfonamides with but few exceptions. Penicillin, like any other medicament, should be employed in sufficient and proper dosage and only when properly indicated."

470. **Abdominal Drainage in Caesarean Section for Infected Cases. (El drenaje abdominal en la operación cesárea del caso impuro.)**
By A. PERALTA RAMOS. *Prensa méd. argent.*, 34, 343–349, Feb. 21, 1947.

471. *d*-Tubocurarine in Caesarean Section.

By T. C. GRAY. *Brit. med. J.*, 1, 444-445, Apr. 5, 1947. 3 refs.

A series of 30 cases in which curare has been used for Caesarean section is reported. Premedication consists of atropine gr. $\frac{1}{100}$ (0.65 mg.) given 1 hour beforehand; when the surgeon is ready the induction is carried out on the table with 15 mg. of *d*-tubocurarine ("tubarine") given intravenously, followed by 0.3 g. of "kemithal" in a 5 per cent solution. Anaesthesia is maintained with cyclopropane in a closed circuit, and respiration is "aided" so that no sub-oxygenation may result from the slight depression of respiration that may occur. Light anaesthesia is maintained until the time of delivery, after which it may be deepened. To build up the carbon dioxide tension in the blood of the foetus and so encourage its initial respirations on delivery, the soda-lime container is cut out of the circuit for a few minutes before the uterus is incised. It is inadvisable to use a pharyngeal airway as it may cause vomiting and retching.

The results are considered encouraging, only 2 of the babies having failed to cry immediately; one of these had received thiopentone instead of kemithal, and the other was premature (32 weeks) with an eclamptic mother; both cried after a short period. There was increased contractility of the uterus and the placenta separated easily; post-operative vomiting and chest complications were minimal; there was no retention of urine, and eye symptoms and ileus were absent. Prostigmine was necessary in 2 cases.

The author considers that this form of anaesthesia fulfils the following criteria : it is safe and pleasant, provides good working conditions for the surgeon, and is not depressing to the child and to the uterine tone. Many of the cases in this series were admitted as emergencies with a consequently increased liability to vomiting during the induction. It is thought that the use of curare not only reduces this liability, but also greatly facilitates intubation should it become necessary. The freedom from curarization of the child is in accordance with the findings of Whitacre and Fisher (*Anaesthesiology,* 1945, 6, 124), and the substitution of kemithal for thiopentone is considered important. In all cases convalescence was uneventful.

[The degree of placental transmissibility of curare has not yet been fully established. Until such time, this method should be used only by experts, and even then only when all the facilities for maternal and foetal resuscitation are at hand. The theoretical possibility of causing premature respirations in the foetus should also be kept in mind when following the practice of building up the maternal carbon dioxide tension shortly before delivery. Good results for "myanesin" in Caesarean section are claimed by Mallinson (*Lancet,* 1947, 1, 98).]

G. C. Steel

472. Postmortem Cesarean Section.

By R. O. JOHNSON and T. V. FRANK. *Amer. J. Obstet. Gynec.,* 53, 343-344, Feb. 1947. 9 refs.

473. The Selection of Forceps for Midpelvic Arrest of the Vertex.

By L. LANGMAN and H. C. TAYLOR. *Amer. J. Obstet. Gynec.,* 52, 773-782, Nov. 1946. 25 refs.

The management of mid-cavity arrest of the vertex has always been a difficult obstetric problem and one which has not been studied statistically. There is no general agreement as to the best type of forceps to use for the delivery of the vertex delayed or arrested in the mid-pelvis. Some believe that once the accoucheur is familiar with one type of forceps he becomes so dexterous with it that he can use it to the exclusion of all other types in every case necessitating forceps delivery; others consider that one type of forceps is not suitable for every case, and that instruments should be available and used according to each particular problem. It has been the practice in the Bellevue Hospital Obstetrical Service, New York, in recent years for the operator to select the type of forceps according to the particular position of the occiput and the architecture of the pelvis. Three types of forceps have been used—the classical (most commonly Haigh-Ferguson), the Barton, and the Kielland.

The material in this study consisted of 701 mid-cavity forceps operations occurring among 10,814 deliveries in the Bellevue Hospital Obstetric Service between Jan. 1, 1934, and Dec. 31, 1945. The factors which influenced the selection of forceps were the experience of the operator with one special type, the position of the occiput, the type of pelvis, and the size of the foetus. When the occiput was anterior the classical forceps was used almost exclusively in the Bellevue Service. In transverse positions of the occiput 75 per cent of

cases were delivered with the Barton forceps, while in 50 per cent of posterior positions of the occiput the Kielland forceps was employed. The Barton forceps became so popular in the Bellevue Service that often posterior positions of the occiput were manually rotated into the transverse or oblique so that this type might be used in preference to the Kielland forceps. As there is a tendency for posterior and transverse positions of the occiput to persist in android and anthropoid pelves, the Barton and Kielland forceps were used predominantly for such cases. The Kielland forceps proved more unsuitable than the others when the foetus was large.

There were 4 maternal deaths in the series of 701 cases, and 3 of these were attributed to the type of delivery, giving a maternal mortality rate of 0.4 per cent for mid-pelvic forceps delivery. The morbidity rate for the series was 41.3 per cent, the standard of morbidity being a rise of temperature to 100.4° F. (38° C.) on at least one occasion on 2 separate days postpartum. The lowest incidence of morbidity was in the group delivered by Haigh-Ferguson forceps.

Type of forceps first applied	Type of forceps with which delivery was completed		
	Classical total cases	Barton total cases	Kielland total cases
Classical 211	183	24	4
Barton 357	30	314	13
Kielland 132	18	9	104

Trauma to the birth canal was most marked when Kielland and Barton forceps were used; 3 vesico-vaginal fistulae, all of which closed spontaneously, were associated with delivery by the Barton forceps. The total foetal mortality, stillborn and neonatal, for the whole series was 9.4 per cent, but the mortality directly attributable to the forceps operation was 5.2 per cent. The foetal mortality associated with Kielland forceps was almost three times greater than that for the Barton and the classical forceps, but the Kielland forceps was preferred in the greater proportion of posterior positions and was employed when one of the other types had been applied unsuccessfully. Delivery was not always possible by the type of forceps first applied, as is seen in the table.

T. N. MacGregor

See also No. 443

MISCELLANEOUS

474. The Trend of Modern Obstetrics.
By E. A. KEELAN. *Irish. J. med. Sci.*, 55–63, Feb. 1947.

475. A Review of 9,000 Obstetrical Cases at the Harris Memorial Methodist Hospital, Fort Worth, Texas.
By G. H. BEAVERS, J. BENNETT, R. L. GROGAN, and C. HIETT. *Tex. St. J. Med.*, 42, 640–645, Mar. 1947.

GYNAECOLOGY

476. Gynaecology in the Women's Services.
By J. MOORE. *Lond. (Roy. Free Hosp.) Sch. Med. Mag.*, 8, 37–41, July–Sept. 1946.

477. Pelvic Examination for Nurses.
By E. ALLEN and C. GALLOWAY. *Amer. J. Obstet. Gynec.*, 53, 290–295, Feb. 1947. 14 refs.

478. Radium and X-rays in the Treatment of Diseases of Women.
By W. T. DINGLE. *Manitoba med. Rev.*, 27, 144–146, Mar. 1947.

479. Study of Some Functional Aspects of Conservative Gynaecology. (Estudio sobre algunos aspectos funcionales de la ginecologia conservadora.)
By W. KOCK. *Bol. Soc. chil. Obstet. Ginec.*, 11, 185–203, Oct., 1946. 14 figs., 14 refs.

480. Effect of Oestradiolbenzoate and Diethylstilboestralpropionate on the Uterus.
(Uber die Wirksamkeit von Ostradiolbenzoat Diäthylstilböstraldipropionat auf den Uterus.)
By E. HUF. *Dtsch. med. Wchsr.*, 72, 84–85, Feb. 14, 1947. 8 refs.

481. Testoviron Implantation in Gynaecology.
(Implantace testovironu v gynaekologii.)
By O. VALENTA. *Ceskoslov. Gynaek.*, 12, 36–48, 1947.

482. Dienestrol. Another Synthetic Estrogen of Clinical Value.
By S. H. SIKKEMA and E. L. SEVRINGHAUS. *Amer. J. Med.*, 2, 251–252, Mar. 1947. 5 refs.

Menstrual Disorders.

483. Control of Menstrual Disturbances and Hypo-ovarian Sterility. Nine Years of Experience with Equine Gonadotropin.
By G. J. HALL. *Amer. J. Obstet. Gynec.*, 53, 259–262, Feb. 1947. 4 refs.

484. Dysmenorrhoea.
By DEWITT D. PHILLIPS. *J. Bowman Gray Sch. Med.*, 5, 27–32, Jan. 1947. 36 refs.

485. Edrisal in the Management of Dysmenorrhea.
By C. F. LONG. *Industr. Med.*, 15, 679–681, Dec. 1946. 5 refs.

" Edrisal " is a tablet containing acetylsalicylic acid gr. 2½ (o.16g.), phenacetin gr. 2½ (o.16 g.), and amphetamine sulphate gr. 1/26 (2.5 mg.). Incorporation of amphetamine overcomes depression and nervous tension which frequently accompany menstruation and, in addition, provides mild analgesia. In a series of 630 women treated with edrisal throughout 1 year, 90 per cent got the relief they sought and lost no time from work.

D. Stewart

486. Dysmenorrhea in Industry—Treatment with a New Antispasmodic.
By F. A. VIGGIANO. *Industr. Med.*, 15, 632–635, Nov. 1946. 17 refs.

A total of 221 patients was treated for dysmenorrhea with " pavatrine ", a comparatively new antispasmodic whose chemical formula is beta-diethylaminoethyl-fluorene-9-carboxylate hydrochloride. It is emphasized that, owing to restrictions placed on the industrial physician, gynaecological examination was not permitted, and the treatment was, of necessity, purely symptomatic. Of the patients 19 were treated during two successive menstrual periods, 1 was treated twice with an interval of 3 days, and 1 during three successive periods, giving a total of 243 courses of treatment. A single dose of two pavatrine tablets (0.25 g. or 4 gr.) was given, followed by a glass of warm water and 1 hour of rest in bed; 76.6 per cent of the patients were able to resume work in 1 hour, 12.7 per cent obtained slight relief and were able to resume work during the same day, while the remaining 10.7 per cent had no relief and were referred to their own physicians for gynaecological examination. These figures compare favourably with those obtained in 128 other patients to whom another antispasmodic was given; only 64 per cent of the latter were able to return to work within 1 hour. The author concludes that pavatrine alleviates dysmenorrheic pains promptly in a high percentage of cases, and that this is of particular importance in the management of dysmenorrhoea in industrial workers.

[The author considers the number of patients sufficient to draw accurate conclusions. There may not be general agreement on this point, as the majority of patients were seen on only one occasion and without any classification of severity of pain.]

A. Lloyd Potter

487. Surgical Treatment of Dysmenorrhea.
By C. J. DUNCAN. *N. Y. St. J. Med.*, 46, 2757–2759, Dec. 15, 1946. 1 ref.

The scope of dilatation and curettage of the uterus and of presacral neurectomy in the treatment of primary dysmenorrhoea is discussed, the author basing his experience on a series of cases at the Brookline Hospital for Women. He favours dilatation and curettage for mild cases and this in conjunction with presacral neurectomy for more serious cases. His operative technique for the latter is the standard one, but a ventro-suspension is done as well [it is not clear whether this is a routine or is performed only in indicated cases]. Sympathectomy gave total relief in 86 per cent in the series of 53 operations [a very high cure rate not always attained]. Secondary dysmenorrhoea usually needs surgical treatment of the pathological lesions present. Radical procedures were favoured in these cases. Presacral neurectomy in this group relieved only 30 per cent of patients.

R. K. Bowes

488. An Evaluation of Presacral Neurectomy in the Treatment of Dysmenorrhea.
By A. W. TUCKER. *Amer. J. Obstet. Gynec.*, 53, 226–232, Feb. 1947. 7 refs.

The operation of presacral sympathectomy has been performed 420 times in the last 14 years at the Free Hospital for Women, Brookline. The author has followed up 255 of these cases in an attempt to assess the value of this operative procedure. Complete relief was obtained in 78 per cent of cases with essential dysmenorrhea and in 33.3 per cent of cases of acquired dysmenorrhea. These results do not give an accurate assessment of the value of presacral sympathectomy, as the author states that " in most cases the operation was routinely combined with a dilatation and curettage, a suspension and any other necessary pelvic surgery which the gynaecologic situation demanded."

Gladys Dodds

489. A Case of Haematometria of Surgical Origin. (Un caso de hematometria de origin quirúrgico.)

By J. A. CARRENO. *Med. Cirug.*, 11, 116–121, Jan. 1947.

490. Effect of Pregneninolone on the Menstrual Cycle of Adolescent Girls with Oligomenorrhoea or Amenorrhoea.

By F. E. HARDING. *Amer. J. Obstet. Gynec.*, 53, 279–284, Feb. 1947. 21 refs.

Zondek and Rozin suggested that in many cases of secondary amenorrhoea it is possible to produce " menstruation " by the use of luteinizing substances injected or taken by mouth. The underlying theory is that many of these patients have already enough oestrogenic hormones circulating. The author has used the oral method with " pregneninolone " (anhydrohydroxyprogesterone) in 46 girls between the ages of 11 and 19 years. In 5 with primary amenorrhoea the treatment failed completely, as was to be expected. The others had suffered from irregular menstruation and before treatment had varying histories of amenorrhoea.

Pregneninolone was administered in doses of 5 to 15 mg. daily by mouth. For irregular menstruation it was given from the eighteenth day of the cycle until the period started. In patients with amenorrhoea treatment was for 10 days each month or continuously till menstruation began. Of patients with amenorrhoea of 3 months' duration or less 87 per cent were improved. The method is not recommended where the interval is longer than 6 months. In general, 40 per cent of the patients continued to menstruate regularly during 6 months after cessation of treatment. In some 70 per cent who also had dysmenorrhoea the condition was relieved.

[It is always difficult to assess the value of reports on the treatment of amenorrhoea. So many factors are involved that treatment verges on the empirical. The results with luteinizing substances do not seem to differ much from those obtained by other methods.]

Kenneth Bowes

491. The Treatment of Amenorrhea and Sterility by X-ray Therapy.

By I. I. KAPLAN. *N. Y. St. J. Med.*, 46, 2746–2752, Dec. 15, 1946. 34 refs.

The author is interested in the radiological treatment of patients who have difficulty in conception and who suffer from amenorrhoea. He now reports

the results of 296 cases treated during 1925–45 and gives more details of the 117 cases seen between 1939 and 1945. The reason for success of this treatment is not fully understood. A disturbance in the balance between the ovaries, the pituitary, the uterus, and the thyroid is postulated, and the X-rays may act on the persisting corpus luteum. There is also evidence that irradiation of the ovaries may influence thyroid action. It is questionable whether irradiation of the pituitary stimulates or not.

High voltage X-rays were used (200 kV. and 10 mA. with 0.5 mm. copper and 1 mm. aluminium filters at 50 cm. distance). Anterior and posterior, right and left pelvic fields were used with 8 × 10 cm. or 12 × 15 cm. portals. The dosage was 50 to 75 r per treatment, given at weekly intervals for 3 weeks. All the patients had irradiation of the ovaries and most of them of the pituitary as well. There had been a gynaecological examination to exclude pelvic abnormalities [the extent of this investigation is not fully stated]. Out of 117 cases treated, 101 were followed up. Eighty-eight patients menstruated regularly; 38 became pregnant, 27 of the pregnancies resulting in normal babies; 3 miscarried; 1 had an ectopic gestation; and 6 were still pregnant.

[This is an interesting paper on a debatable subject. Unfortunately neither the statistics nor the clinical details are made very clear, as two overlapping series of patients are quoted.]

R. K. Bowes

492. Amenorrhoea in the Ghetto. (Die Ghetto-amenorrhoe.)

By J. NOCHIMOWSKI. *Med. Klinik.*, 41, 347–348, Aug. 1946. 2 refs.

When Kovno was overrun by the Germans 30,000 Jews were shut up in the Ghetto at once. Among a number of the females there was a sudden cessation of the menses [the incidence is not given], to which the author gives the name " Ghetto-amenorrhoea." The usual physical concomitants of prolonged amenorrhoea were not seen, nor was there an increase of weight in the subjects. Pregnancy occasionally occurred. Libido was at first diminished, but was later greatly increased. Nothing abnormal was found on physical examination. After about nine months, when the community had more or less adapted itself to its altered

living conditions, menstruation began again with dramatic suddenness and intensity. Haemorrhage was profuse, lasting for a week, and was accompanied by intense pain in the abdomen and back. Subsequent menses were normal, and the women felt well and sometimes found that previous menstrual disturbances had now vanished.

The theory is advanced that the acute psychic trauma led to an overaction of the thyroid (hyperthyroidism was often seen in the Ghetto), that this caused a compensatory increase in production of follicular hormone, and that with the passing away of the psychic trauma and the consequent fall in production of thyroid hormone a sudden imbalance between the levels of thyroid hormone and follicular hormone in the blood led to the menorrhagia observed.

Josephine Barnes

493. Ovarian Swelling and Intraperitoneal Bleeding as a result of Gonadotrophin Treatment. (Svulne Ovarier med Blodning i Bughulen som Folge af Behandling med Gonadotropiner.)
By H. C. PETERSEN. *Ugeskr. Læg.*, **108**, 1351–1352, Nov. 28, 1946. 1 ref.

A nullipara, 21 years old, received two courses of treatment with gonadotrophins at 3-year intervals for hypo-oligomenorrhoea. Soon after the last course—15,000 units of " antex " and 4,500 units of " physex "—she developed acute abdominal pain with a palpable suprapubic tumour. At operation, a half-litre of blood was found in the abdomen; both ovaries were cystic and of a jelly-like consistency with infiltration of blood which had ruptured the capsule, one ovary being the size of a foetal head and the other the size of a fist. Resection of the former and suture of the latter were performed. Subsequent progress was uneventful.

494. Mixed Synthetic Estrogens—Their Use in the Menopause. (Dimethoxy Stilbestrol and Diethylstilbestrol.)
By O. H. BLOOM. *Amer. J. Obstet. Gynec.*, **53**, 263–265, Feb. 1947. 1 fig., 1 ref.

The disadvantages of treatment by repeated oral doses or by implantation of pellets of oestrogens are well appreciated. The author of this article has tried to overcome them by using a combination of stilboestrol and dimethoxystilboestrol in an oily solution. The dimethoxy product has to be demethylated to produce a response in the body

and hence gives a prolonged action. There is an immediate response to stilboestrol which tides the patient over until the other product can act. Injections of 15 mg. of dimethoxystilboestrol and 1 mg. of stilboestrol in an oily solution are given weekly for three consecutive weeks. There appears to be genuine synergic action. The patient is free from symptoms [and treatment] for 4 months. In 56 patients observed, there were no toxic reactions; withdrawal bleeding occurred in 3 cases.

[This appears worthy of further trial.]

Kenneth Bowes

495. Pathologic Findings in Genital Bleeding Two or More Years after Spontaneous Cessation of Menstruation.
By D. B. CHEEK and J. E. DAVIS. *Amer. J. Obstet. Gynec.*, **52**, 756–764, Nov. 1946. 1 fig., 12 refs.

The results of a study of 514 cases of postmenopausal bleeding occurring in the Johns Hopkins Hospital over a period of 7½ years are recorded. No case was included in this study unless 2 years had elapsed since the last menstrual period. Patients referred for treatment for proved carcinoma were excluded. The complete investigation to which all cases, with few exceptions, were subjected included: (a) general physical examination, (b) gynaecological examination, (c) digital examination of anus and rectum, (d) urological survey, (e) haematological study, (f) biopsy of cervix, and (g) curettage of the uterus. The causes of the bleeding are tabulated below:

Pathological Findings According to Location.

Vulva:

Carcinoma	2
Melanosarcoma of clitoris	1
Ulcer, non-specific (not granuloma) ...	2

Urethra:

Carcinoma	5
Caruncle	10
Prolapse	2
Urethritis	1

Vagina:

Carcinoma	1
Vaginitis, senile	60
Granuloma inguinale	1
Trauma	5
Pessary	5

Carried forward   95

	Brought forward	95
Cervix:		
Carcinoma		104
Polyp		37
Prolapse		35
Cervicitis, marked		36
Uterus Corpus:		
Carcinoma		58
Sarcoma of endometrium		2
Sarcoma in myoma		2
Myoma, submucous		18
Polyp, endometrial		18
Hyperplasia of endometrium		20
Endometritis, pyometra		6
Fallopian tube:		
Carcinoma		1
Tuberculosis		1
Ovary:		
Malignant		
Papillary cystadenocarcinoma 3		
Medullary carcinoma ... 1		9
Krukenberg tumour ... 2		
Granulosa-cell tumour ... 3		
Benign		
Papillary serous cystadenoma 1		
Serous cystadenoma ... 1		4
Pseudomucinous cystadenoma 2		
Bleeding probably from oestrogen therapy ...		12
Unknown cause, including 7 cases with probable recrudescence of ovarian function		56
Total		514

The authors emphasize the importance of a complete study of every case of post-menopausal bleeding irrespective of any obvious cause found on superficial examination. Out of the total of 514 cases 185, or 36.1 per cent were due to malignant growth and 329, 63.9 per cent to benign. When these figures are compared with those of similar surveys tabulated by the authors it is seen that the incidence of malignancy in the present series studied is considerably lower.

In analyzing their data the authors found that there was no significant racial difference in regard to aetiology, except that bleeding associated with prolapse of the cervix was uncommon in the negro race. The average age when the menopause was reached was 47.8 years, and when the age-groups are examined in relation to malignancy it is seen,

as would be expected, that with increasing age there is a greater proportion of malignant lesions. The average duration of amenorrhoea for the entire series was 10.1 years. There was no correlation between the time the amenorrhoea had lasted and the cause of the bleeding, nor was the duration or type of bleeding in any way related to the causative lesion.

T. N. MacGregor

496. Orientation in Gynecologic Uterine Bleeding.
By C. E. McLENNAN. *Journal-Lancet*, **67**, 90–93, Mar. 1947. 5 refs.

497. Postmenopausal Bleeding.
By C. MACFARLANE. *Penn. med. J.*, **50**, 598–601, Mar. 1947. 2 figs.

498. Radium and Roentgen Therapy in the Treatment of Menopausal Uterine Bleeding.
By H. E. SCHMITZ and J. E. TOWNE. *Amer. J. Obstet. Gynec*, **53**, 199–206, Feb. 1947. 1 fig., 8 refs.

Sterility.

499. Sterility in the Female. Uterosalpingography and Resection of the Ovary. (Esterilidad femenina. Uterosalpingografía y resección ovárica.)
By R. PERALTA. *Med. Cirug.*, **11**, 101–116, Jan. 1947. 3 refs.

500. Pregnancy following Hysterosalpingography with Unconfirmed Tubal Patency. (Gravidanze successive ad isterosalpingografia con pervietà tubarica non accertata.)
By E. ROBECCHI. *Ginecologia*, **12**, 173–188, July-Aug. 1946. 45 refs.

The author considers that hysterosalpingography, in addition to its diagnostic value, has a therapeutic use in cases of sterility. Reports in the literature mention figures of up to 42 per cent of pregnancies after this procedure, in the majority of which the subject had previously been sterile. The author analyzes his feelings in 1,000 salpingographies. He has found that pregnancy subsequently occurs in 15 per cent of cases with normal tubal patency, 5 per cent of cases of unilateral tubal occlusion, 9.9 per cent of cases of impaired patency, and 9 per cent of cases of tubal occlusion. The author finds difficulty in explaining this fact. He considers that pregnancy may have followed the dilatation of the cervix or may have been aided by the active contraction of uterine and tubal muscle in response to the stimulus of the iodized oil. In addition, the

pressure of the oil may have freed the lumen from an obstacle. By increasing the pressure and maintaining oil within the tubes for a period of up to 2 hours he has often obtained filling of tubes previously regarded as occluded. Lipiodol (40 per cent). is introduced and maintained at a pressure of 200 ml. of mercury for 2 hours. In no case was any ill effect seen. Case reports are given of 5 patients who had an apparently complete obstruction and subsequently became pregnant, and of 5 other cases in which patency had been doubtful. The following factors which may lead to an incorrect diagnosis of sterility are mentioned. (1) It is recommended that the examination should be carried out at the time of maximal physiological permeability of the tubes. (2) A stenosis of the tubal lumen may be incorrectly interpreted as an occlusion. In such cases air insufflation may lead to the correct diagnosis. (3) Hypotonus of the uterine muscle may account for inadequate filling of healthy tubes. In such cases the atonic uterus appears to be pear-shaped and has a capacity of 6 to 8 ml. Contractions at the isthmus and the tubal angles are not seen and the emptying of the oil is prolonged. The use of drugs which provoke uterine contraction—for example, carbachol—is recommended. (4) Hypertonus is a more frequent finding, particularly in infantile and deformed uteri. Spasm may be responsible for the insufficient injection of the tubes. In these cases the giving of antispasmodics at least half an hour before the examination may help. (5) The oily solution, especially if of low concentration, may be quickly absorbed, so that the 24-hour film suggests an occluded tube. The above points are illustrated by case reports.

Hilde Eisner

501. **Tubal Sterility. Results of Operations.** (La stérilité tubaire. Résultats opératoires.)
By E. DOUAY. *Paris méd.,* 36, 568–575, Dec. 21, 1946. 6 figs.

During the last 20 years the author has performed conservative operations on 64 sterile women, 27 on hospital patients and 37 in his private practice. The results in his hospital patients have been disappointing, no case of subsequent pregnancy having been recorded, but in his private practice 6 pregnancies leading to the birth of living children have followed (2 to the same woman) and one abortion. The disparity is possibly due to the poor follow-up in the hospital series, since pregnancy may occur long after a conservative operation for sterility. The preoperative examination must always include tubal insufflation and hysterosalpingography. At laparotomy, lesions may be much more extensive than investigation has indicated but hysterectomy should only be performed when absolutely necessary, since most patients prefer to cling to an even infinitesimal chance of becoming pregnant.

In the present series the operations are grouped as: (1) salpingostomy for adhesions at the fimbriated end of the tube; 10 operations, 4 pregnancies; (2) partial salpingectomy; 16 operations, no pregnancy; (3) tubo-uterine anastomosis; 2 cases, 1 pregnancy; (4) ovarian implantation into uterus; 6 cases, one abortion. The case histories of the successful operations are given in detail and the fact that emerges is the efficacy of early operation before permanent pathological changes have occurred in the mucosa and muscle of the Fallopian tube.

S. S. B. Gilder

502. **Surgical Treatment of Tubal Sterility.** (Tratamento cirúrgico da esterilidade tubária.)
By A. CAMPOS da PAZ FILHO. *Rev. Ginec. Obstet.,* 40, 286–294, Nov. 1946. 5 figs., 17 refs.

A successful salpingostomy for secondary sterility is described. The authors state that, in their opinion, the indications for this operation are very restricted (only 1 was performed out of a series of 296 cases of sterility investigated). The patient became sterile after an induced abortion 3 years earlier. She had a hydrosalpinx on the left side and an obstruction without dilatation at the fimbrial end of the right Fallopian tube. Salpingostomy with eversion of the tubal mucosa was performed at the abdominal ostia. Oestradiol benzoate, 1 mg. weekly, was injected post-operatively and prolonged short-wave therapy was also given. A hysterosalpingography showed that both Fallopian tubes were now patent. Eight months after operation, pregnancy which ended in abortion occurred, and a year later a normal pregnancy ended in the birth of a live child.

S. S. B. Gilder.

503. **Examination of Semen in Childless Marriages.** (Spermieundersokelse ved ufruktbare ekteskap.)
By M. SVENDSEN. *Tidsskr. Norske Laegeforen.* 67, 11–13, Jan. 15, 1946. 1 ref.

After a brief mention of the history and the background of the subject, the author gives an account of the normal and abnormal findings in semen and their interpretation. It is estimated that about 10 per cent of marriages in Norway are childless and that probably this is a matter of choice in less than half.

Fresh ejaculate is described and attention drawn to the presence of blood (found in tuberculosis and tumours) and threads of mucus (found in prostatitis and vesiculitis). The volume comes mainly from the secretions of accessory glands and depends chiefly on the interval since the last ejaculation, but after 3 days should be at least 1.5 ml. Spermatozoa should be actively motile, but even in fertile men the proportion after half an hour may be as low as 40 per cent. Non-motile spermatozoa are assumed to be incapable of fertilization, but it must be remembered that motility is inhibited by hypotonic solutions, acidity (semen is weakly alkaline but the vaginal secretions are acid), and local disease. Semen without any motile spermatozoa is the cause of sterility in only 2 per cent of cases. The concentration of spermatozoa depends partly on the interval since the last ejaculation, but should be at least 60 million per ml. It is depressed with varicocele, in orchitis, and in a group of cases with soft testes and markedly abnormal heads in the spermatozoa. It is not altered in syphilis or gonorrhoea unless there is a stricture. Aspermia is found in testicular insufficiency and where there is obstruction to the channels of discharge. It is claimed by other authors to be the cause of 9 to 30 per cent of childless marriages; the author found it so in 14 per cent.

The morphology of the spermatozoa is very important, but up to 20 per cent of abnormal forms are found in fertile men. The commonest abnormality is a pyriform head, which is classed by some as an immature form and may occur in 20 per cent of the spermatozoa of fertile men. Another type is the round-headed spermatozoa. Hammen claims that areas of congenital hypoplasia can be demonstrated in almost every human testis, and suggests that round-headed forms are derived from these areas. A third type is the abortive form with undifferentiated head and lumps of cytoplasm or with a bent middle section. A fourth group contains the pathological forms—dwarfs, giants, those with many heads, and those with none. If the abnormal forms make up over 20 per cent they are usually either mainly round-headed and double forms, or mainly abortive and pyriform. The abnormalities are relatively constant for the individual and not affected by age. White blood cells may be found, often in association with a high percentage of pathological forms, but cultures are sterile.

The number and degree of abnormal findings indicate the likelihood of infertility: absolute sterility should be inferred only if repeated examinations show aspermia. Hammen found some abnormality affecting fertility in nearly all the wives, and abnormalities in the sperm of 53 of the husbands, in a series of 100 childless marriages. It is pointed out that the chance of having children is affected by the abnormalities on both sides, and that if the man has a poor ejaculate minor abnormalities, perhaps quite temporary, in the woman may be highly important and vice versa.

A. M. M. Wilson

504. Contraception Masking Sterility and Infertility. Tubal and Seminal Factors in 1,000 Cases. By I. C. RUBIN. *J. Amer. med. Ass.*, **132**, 1047–1053, Dec. 28, 1946. 1 ref.

The author points out that the use of contraceptive methods is not infrequently resorted to by married couples who are actually sterile and in whom therefore contraception is unnecessary. Furthermore, as the couples do not know they are sterile treatment to cure sterility is not undertaken in the period soon after marriage, when it has a better chance of success than when delayed, as it often is, for a number of years. This applies both to cases of primary sterility where the patient has never conceived, and to cases of secondary sterility where contraception has been employed for varying lengths of time after one childbirth or after one or several spontaneous or induced abortions.

In the present paper the records of 1,000 cases of sterility have been analyzed to determine to what extent " reproductive stigmas " were present in the group of women who practised contraception as compared with those who did not. There were 711 cases of primary sterility and 289 of secondary sterility. In the former group, there were 466 couples who had used contraception during the first part of married life and 212 who had not. In 33 cases information was lacking.

In the examination of the records of the 466 couples who had practised contraception the major sterility factors were studied. This consisted in physical examination of wife and husband, utero-tubal insufflation, examination of semen, and determination of basal metabolic rate where indicated. The aetiological factors fell into 4 groups: (1) abnormalities of the pelvic organs; (2) endocrine dysfunction; (3) seminal inadequacy; and (4) tubal impairment. Bimanual examination with routine use of the vaginal speculum sufficed in most cases to determine the presence or absence of gross pelvic abnormalities. In a few, hysterography was used. The evaluation of endocrine dysfunction was limited to consideration of : (a) ovarian dysfunction as shown by amenorrhoea, hypomenorrhoea, oligomenorrhoea, menorrhagia, and metrorrhagia; and (b) hypothyroidism as demonstrated by a diminished basal metabolic rate.

In most cases Hubner's test was used for the study of semen, checked when necessary by examination of one or several samples brought in a glass container. The tubal status was determined by utero-tubal insufflation with carbon dioxide gas. Abnormalities of the pelvic organs or diseased conditions capable of diminishing fertility were found in 28.5 per cent. These included uterine hypoplasia, fibromyomata, retroversion, and cervical stenosis. As regards endocrine dysfunction, there were 19 women with menstrual difficulties and 15 with hypothyroidism, a total of 34 (7.3 per cent). Seminal inadequacy (azoospermia, necrospermia, or decided oligospermia) was judged to be present in 46.2 per cent. It is concluded that absence of spermatozoa by the Hubner test, even on several occasions, is not always conclusive evidence of male sterility, for normal spermatozoa may be demonstrable in the semen itself. Neither is absence of motility of the spermatozoa in the vaginal or cervical secretions 1 or 2 hours after coitus an absolute sign of infertility, for 47 out of 101 women in this series have become pregnant despite repeated evidence of non-motility.

Tubal status was determined in 353 of the 466 women; 51.6 per cent showed evidence of impairment. Of these, 21.3 per cent had non-patent tubes after several tests, 19.8 per cent had partially patent (from stricture or peritubal adhesions), and 10.5 per cent had spastic. To what extent the tubal impairment was present at marriage or acquired afterwards was not possible to determine.

Infertility factors were thus present in 80.3 per cent of the 466 women. This incidence might, however, be unduly high, as many of the cases had been of long standing or had proved refractory to all previous therapeutic measures—in short, they were a selected group. The seminal and tubal factors were the ones most often encountered, and this emphasizes the importance of a thorough examination of the semen and the tubal status. It should be noted that a prognosis cannot be given on any one specimen of semen. " At the present time one can only speak of the morphological characteristics, of estimated numbers of spermatozoa, and of the degree and type of motility. Actual insemination repeated over a certain length of time is necessary in order to determine its compatibility and ultimate fertility." In the group of 212 couples who did not use contraceptives the incidence of pelvic abnormalities, endocrine dysfunction, seminal inadequacy, and tubal impairment was substantially the same as in the first group.

The wisdom of determining the potential fertility of couples seeking contraceptive advice before such advice is tendered is discussed. The sooner the causal factor is determined and eliminated the better the prognosis; when the factor cannot be overcome it is better for the couple to know the facts as soon as possible. Unnecessary contraception may then be discontinued, psychological adjustment made, and, if desired, steps may be taken to adopt a child or for impregnation by a donor. In this series, however, it was estimated that only about 40 per cent had sought medical advice before practising contraception.

<div align="right">F. J. Browne</div>

Abnormalities of the Reproductive Organs.

505. **Double Sclerosis of the Vagina.** (Eine Doppelsklerose der Vagina.)
By V. GRUENBERGER. *Wien. med. Wschr.*, **97**, 113–115, Mar. 8, 1947. 2 figs., 2 refs.

506. **A Case of Congenital Absence of the Vagina.**
By J. H. HANNAN. *Med. Press*, **217**, 270–271, Apr. 2, 1947.

507. **Bilateral Ovarian Aplasia.**
By C. A. ERSKINE and I. RANNIE. *Arch. Path., Chicago*, **42**, 381–390, Oct. 1946. 6 figs., 25 refs.

To the 6 undoubted cases of primary bilateral aplasia of the ovaries on record these authors add a seventh, which occurred in a white unmarried woman, aged 35 years, who died from pulmonary and abdominal tuberculosis. Clinically there was primary amenorrhoea with absence of secondary sexual characteristics. Necropsy showed that, although the genitalia were essentially female, they were not developed beyond the stage of pre-puberty: there was complete absence of ovaries and no ectopic ovarian tissue was discovered. Histologically the tubes showed only evidence of recent tuberculosis. The epoophoron was carefully examined and resembled the normal in all essential aspects. One block contained a number of pigmented (iron-free) cells which were regarded as interstitial cells. The uterus, vagina, and breasts were all hypoplastic. The suprarenals were rather small and so was the thyroid, and its vesicles were filled with resting colloid. There was physiological involution of the thymus, but the pineal and pituitary glands showed no gross difference from normal.

The authors compare the findings in their case with those in the others recorded and summarize the main features in which they all agree. Variations do occur but are of minor importance, and the conclusion is reached that no specific changes in the other endocrine organs attributable to the absence of the ovaries can be found. Commenting upon the case, the authors discuss sex determination in relation to the primordial sex cells and their effect on the genital ridge. The influence of hormones on the further sexual development of the individual is also mentioned, and the opinion is formed that the usual genetic view of sex determination is actually supported by the occurrence of cases of bilateral ovarian aplasia.

R. B. T. Baldwin

See also No. 411.

Infections of the Reproductive Organs.

508. Clinical Evaluation and Analysis of 268 Cases of Pelvic Infection.
By I. TRACTENBERG. *J. int. Coll. Surg.*, 9, 724–728 and 741, Nov.–Dec. 1946.

Some of the clinical features and the general lines of treatment adopted in the author's series of 268 cases of pelvic infection in women are discussed. The three main causes of pelvic infection

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are gonorrhoea, puerperal infection (pyogenic organisms, usually streptococci and staphylococci), and tuberculosis. Pyogenic infection is essentially a wound infection and spreads mainly by lymphatics, the characteristic lesion being a pelvic cellulitis; gonorrhoea is an infection to the mucous membrane of the genital tract and is an ascending infection to the mucosa of the tubes, whence it may spread through the other coats.

In this series infection was gonorrhoeal in 90 per cent of cases. Conservative treatment, including sulphathiazole, was used for all acute cases, and surgery was only indicated for drainage of an abscess. In subacute and chronic cases heat in the form of vaginal douches was used in addition to other measures. Posterior colpotomy was performed for residual pelvic abscesses; where abdominal operation was required both Fallopian tubes usually had to be removed, in which case a subtotal hysterectomy was done in addition. The mortality was 2.2 per cent.

[This article is written in too general terms to be of great value in assessing the merits of treatment].

L. W. Lauste

509. Microbiology of Vaginal Flora. (Mikronini obrazy posevní.)
By O. JIROVEC, R. PETER, and I. MALEK. *Ceskoslov. Gynaek.*, 12, 1–24. 1947. 22 figs.

510. Presence and Significance of the Anaerobic Vaginal Flora. (Vyskyt a vyznam anaerobní posevní flory.)
By F. PATOCKA and V. SEBEK. *Ceskoslov. Gynaek.*, 12, 24–36, 1947.

511. A Study of the Bacterial Flora of the Normal and Pathologic Vagina and Uterus.
By K. E. HITE and L. GOLDSTEIN. *Amer. J. Obstet. Gynec.*, 53, 233–240, Feb. 1947. 32 refs.

512. The Treatment of Mycotic Vulvovaginitis with Propionate Vaginal Jelly.
By R. L. ALTER, C. P. JONES, and B. CARTER. *Amer. J. Obstet. Gynec.*, 53, 241–244, Feb. 1947. 5 refs.

Mycotic vulvo-vaginitis is a common condition. A number of treatments have been tried with some degree of success, but all have the disadvantage that they are time-consuming for the patient and physician because applications have to be made two or three times weekly to the cervix, vagina,

and vulva. The treatment used by the writers, at Duke Hospital, Durham, N.C., has a high rate of cure and can be applied by the patient herself. The fungistatic substance employed is a propionate, in a jelly-like mixture, the formula of which is: Calcium propionate, 9.5 per cent; sodium propionate, 9.5 per cent; propionic acid, 1 per cent; glycerin, 10 per cent; " bentonite ", 32 per cent; water, 38 per cent. The jelly is supplied in tubes with an applicator which holds 8 to 10 ml. The patient inserts the applicator, which is full of jelly, into the vagina, and deposits the contents in the upper vagina night and morning. Treatment is necessary for two or three weeks.

Gladys Dodds

513. Hydrogen Ion Concentration (pH) of the Vagina Associated with an Ectropion of the Cervix (Cervicitis).
By K. J. KARNAKY. *Amer. J. Surg.*, 73, 359-362, Mar. 1947 2 refs.

514. Syphilis of the Cervix.
By W. F. GUERRIERO, W. B. MANTOOTH, and W. MOORE. *Sth. med. J.*, 40, 261-264, Mar. 1947. 9 refs. .

515. The Present Status of Endocervicitis.
By C. PANETTIERE. *Sth. med. J.*, 40, 183-186, Feb. 1947.

This paper assesses the present status of endocervicitis and suggests a method for the treatment of this condition and of erosion of the cervix. The author states that 75 per cent of the adult female population is affected by this condition; his conclusions are based upon the observation of patients in South Florida, who come from all sections of the United States and the West Indies, representing a fair cross-section of the women of these countries. The lacerated cervix, malignancy of the cervix, and the postpartum cervix are not considered in his report. The outstanding manifestation of endocervicitis and erosion is a vaginal discharge, a symptom common to many diseases of the cervix and adnexa. The aetiological factors at work in the production of the condition are considered to include infection, hormonal influences, and abnormal anatomical positions of the uterus. In treatment the author employs a method which he considers the most satisfactory of the many he has used. The vaginal vault is

thoroughly irrigated with a solution of warm mercury cyanide and the surface dried with gauze on a sponge holder. If the cervical canal is plugged with mucus—as is often the case—the plug is removed. The whole area is then sprayed with a 1 in 1,000 tincture of " merthiolate," followed by a generous spraying with " flumerin." Flumerin is a disodium salt of hydroxymercuri-fluorescein, containing 30 to 32 per cent of mercury in organic combination. Enough is left in the vault to saturate a small gauze tampon, and this is left for 24 hours in apposition to the cervix before removal by the patient. Local treatment of this nature is repeated twice weekly for an average duration of 3 weeks. At the end of that period the discharge has usually disappeared or has greatly diminished, and complete epithelization follows spontaneously. No contra-indication to the method, and no evidence of mercurial absorption, have been discovered.

Falkland L. Cary

516. Torsion of Hydrosalpinx. (Les hydrosalpinx tordus.)
By G. LEGRAND. *Brux. méd.*, 27, 715-719, Mar. 30, 1947. 2 figs.

New Growths of the Reproductive Organs.

517. Leucocytic Variations after Short-wave Applications in the Gynaecological Field. (Variazioni leucocitarie dopo applicazione di onde corte nel campo ginecologico.)
By T. M. CAFFARATTO. *Ginecologia, Torino*, 12, 237-248, Sept. 1946. 37 refs.

518. Certain Pelvic Tumours Associated with Ascites and Hydrothorax.
By M. CALMENSON, M. B. DOCKERTY, and J. J. BIANCO. *Surg. Gynec. Obstet.*, 84, 181-191, Feb. 1947. 5 figs., 57 refs.

While the syndrome of ascites and hydrothorax associated with fibroma of the ovary has been described in medical literature from 1879, the syndrome was little known until the report by Meigs in 1937. The authors review the literature on this subject over a period of 60 to 65 years. They consider that the time has come (as Meigs and others anticipated) to include in the syndrome not only ovarian fibromata but also other benign and even malignant ovarian tumours. [They quote 2 published cases of recovery following removal of ovarian cystadenocarcinomata associated with

hydrothorax and ascites. The malignant nature of the tumour in itself was, therefore, not the cause of the ascites and hydrothorax.]

In the Mayo Clinic approximately 20,000 pelvic tumours were removed from 1910 to 1945. In 9 cases associated ascites and hydrothorax were also present. A tenth case was seen in 1946. The average age of these 9 was 48 years (extremes 36 and 67). Parity did not appear to be related to the development of the syndrome. Abdominal enlargement was the commonest complaint. The tumours found were 4 ovarian fibromata, 1 ovarian fibromyoma, 1 degenerating uterine fibromyoma, 1 fibromyoma of uterus with pelvic inflammatory adnexal disease, 1 granulosa-cell tumour of the ovary and 1 complex teratoma of the ovary. The tenth was a cystic fibroma of the ovary. The end-results of surgical treatment in all 9 cases (the result in the tenth is not discussed) were excellent. Neither ascites nor hydrothorax recurred. (The longest follow-up was 27 years.) Theories of the aetiology of the ascites and hydrothorax in this syndrome are discussed *in extenso*.

Anthony W. Purdie

519. **Prevention of Female Genital Cancer.** (Prevençao do câncer genital femino.)

By A. H. ROCHA. *An. brasil. Ginecol.*, 22, 467-473, Dec. 1946. 4 refs.

520. **Carcinoma of the Vulva. Results of Treatment and Effect of Special Factors on Results.**

By F. R. SMITH and R. S. POLLACK. *Surg. Gynec. Obstet.*, 84, 78-84, Jan. 1947. 1 fig., 21 refs.

The authors discuss a series of cases of carcinoma of the vulva treated in the Memorial Hospital, New York, from 1926 to 1945. Of 244 cases, 167 were primary and 77 cases had received previous treatment. Of the primary cases 100 have been observed for a period of 5 years or more and evaluation of the results of treatment is based on these. Although carcinoma of the vulva accounts for only 4 per cent of all cases of malignancy in the genital tract, it is important because it provides an opportunity for early diagnosis and even prevention; the poor results, however, indicate a failure to take adequate advantage of these facts. The growth is essentially a skin carcinoma, but presents special features owing to the anatomy and rich lymphatic drainage of the vulva.

In this series the youngest patient was 27 years old, and the oldest 89 years, the main incidence occurring in the 60 to 69 age-group; 86 per cent were married or widows, and 14 per cent single; 75 per cent had one or more children, and 25 per cent were nulliparous. Eight of the patients had syphilis and 10 diabetes, but these conditions did not appear to be of significance. Pruritus, pain, and bleeding were the common symptoms, and 70 per cent of the patients presented themselves because of the lesion. The authors stress the importance of pruritus as a symptom which occurs in over 50 per cent of patients, and state that 36 per cent of the patients had leucoplakia. Histologically, 89 cases were of epidermoid carcinoma, 25 of melanoma, 9 of basal-celled carcinoma, 1 of adenocarcinoma of Bartholin's gland, 1 of vulvar Paget's disease, and 1 of dermatofibrosarcoma protuberans. Thus 84 per cent were epidermoid carcinomata and two-thirds of these were grade II carcinoma. The percentage of melanoma was unduly high.

In the period 1926-40 there were 100 cases of primary carcinoma and 46 cases previously treated. The absolute 5-year cure rate in both groups was 26 per cent. The cases were also analyzed in various sub-groups to determine the influence of different factors on end-results. These groups were: (1) Cases with involvement of the lymph nodes: A, clinically; B, histologically. (2) Cases with involvement of the lymph nodes and operable; A, clinically; B, histologically. (3) Inoperable cases. Graphs of the survival rates of these groups showed the highest rate to be in Group 1 B (80 per cent) with a marked fall in Group 2 (about 10 per cent of 5-year survivals) and no 5-year survivals in Group 3.

All cases were treated by surgery, X-rays, or radium, or by a combination of these methods. Surgical treatment included simple vulvectomy, vulvectomy with excision of the nodes on one or both sides, and vulvectomy with a Bassett type of node dissection. The results show that the prognosis is much worse if the lymph nodes are involved, and indicate the advisability of removing them. The results in cases treated with X-rays alone or by vulvectomy with X-rays or radium were less good than those obtained by surgery. It was possible in most cases to determine the site

of origin of the growth, and it appeared that the prognosis was least good in growths of the clitoris; 59.6 per cent occurred in the labia majora, 21 per cent in the labia minora, 27 per cent in the clitoris, and 3.8 per cent in the region of the posterior commissure. The prognosis was worst with melanoma and best with basal-celled carcinoma and epidermoid carcinoma of Grade I. The cases previously treated were analyzed separately, and the general findings were in keeping with those of the primary group, the absolute 5-year survival rate being exactly the same—namely, 26 per cent.

It is concluded that in all cases suitable for surgery, vulvectomy with dissection of the lymph nodes should be done. It was not possible to say whether the Bassett type of dissection had any advantage nor, from the figures, could it be judged whether a one-stage or multiple-stage operation was best. In view of the malignancy of melanoma it was considered advisable to remove all pigmented tumours.

                                            L. W. Lauste

521. Fibroadenoma of Supernumerary Mammary Gland Tissue in Vulva.

By J. H. FISHER. *Amer. J. Obstet. Gynec.*, 53, 335–337, Feb. 1947. 2 figs., 7 refs.

522. A Case of Bowen's Disease of the Vagina. (A propos d'un cas de maladie de Bowen vaginale.)

By J. FIGARELLA. *Rev. franç. Gynéc.*, 41, 347–351, Nov. 1946.

Bowen's disease of mucous membranes occurs in women aged 40 to 73; it is slowly progressive, lasting on the average 11 years; the aetiology is unknown, but it occasionally follows kraurosis vulvae; it may be situated anywhere in the mucosa of the genital tract. The earliest lesion is a small papule, which gradually increases in size and multiplies. Many consider it to be a precancerous condition. It must be distinguished from syphilitic, tuberculous, and diabetic lesions, but the only condition which is very difficult to differentiate from Bowen's disease is the " erythroplasia of Queyrat " or " denuded papillary epithelioma of Darier "; in fact, this last dermatosis and Bowen's disease may be two different aspects of the same condition. Bowen's disease of mucous membranes was first described in 1921 by Jessner, who published 2 cases. Since then several cases have been published. Of all cases of Bowen's

epitheliomatous dyskeratosis, about 22 per cent are situated in mucous membranes. The author describes a case in a 61-year-old patient, who complained in 1942 of blood-stained vaginal discharge for 4 months, with no pain but with lower abdominal discomfort. The menstrual history was normal; 10 pregnancies had resulted in 5 miscarriages and 5 deliveries. The perineum and vulva were healthy, the uterus and adnexa normal. The vaginal wall was covered by small granular elevations, quite smooth, red in colour, and there was a serous blood-stained exudate. Biopsy demonstrated very hypertrophied epithelium, undifferentiated Malpighian cells—many of which showed mitosis, some atypical and some with giant nuclei; the submucous layer was normal. The lesions were cauterized and apparently healed, but have gradually returned and now, 3 years later, are just as abundant without exhibiting any malignant change.

                                    Nicolas Tereshchenko

523. Modern Trends in the Management of Uterine Carcinoma.

By F. L. PAYNE and G. L. HOFFMAN. *Penn. med. J.*, 50, 491–496, Feb. 1947. 38 refs.

524. The Vaginal Smear. Practical Applications in the Diagnosis of Cancer of the Uterus.

By J. V. MEIGS. *J. Amer. med. Ass.*, 133, 75–78, Jan. 11, 1947. 6 refs.

The use of smears from the vagina in the diagnosis of uterine cancer is reviewed by the author, who has experience of 2,749 examinations in the Massachusetts General Hospital, in which series the method gave an error of only 3.2 per cent.

Detailed technique is given by Papanicolaou and Traut (*Amer. J. Obstet. Gynec.*, 1941, 42, 193). Briefly the method consists in aspirating vaginal secretion into a glass tube with a rubber suction bulb and blowing the secretion on to a glass slide, then spreading the secretion into a thin film and fixing immediately in equal parts of ether and 95 per cent alcohol. The film is subsequently stained. Diagnosis depends on recognition of abnormal nuclear pattern in shed cells and demands of the pathologist considerable experience of the technique, besides being a time-consuming procedure. Additional help may be obtained from the presence of leucocytes and red cells in the smear. This method is preferred to more elaborate ones which

use endocervical catheters, as its simplicity brings it within the range of the general practitioner. Moreover, the vaginal secretion contains cells derived from the entire uterine mucosa and so may be more accurate.

The diagnosis by smear of cancer of the cervix is simple, as cancer cells are unmistakable. False positive results (amounting to 2 per cent of the author's series) are probably explained by early growths being missed in serial sections after hysterectomy. False negative results were obtained in 3.5 per cent of cases of cervical cancer, and are to be explained either by the growth not shedding cells or by preliminary douching by the patient. In endometrial cancer confusion between malignant and non-malignant cells in smears is not infrequent, and more expert observation is thus demanded. False negatives were obtained in 20 per cent of the author's series of 80 endometrial cancers.

The author regards this method as of proved value in making an early diagnosis of uterine cancer. Of his series of 339 cases of this condition, in 25 cases early diagnosis depended upon or was materially assisted by vaginal smears. It is particularly valuable in following up cases of cancer previously treated by irradiation, although diagnosis in such cases is more difficult than usual. It is emphasized that this method can be more accurate than biopsy, but radical surgery on the strength of positive smears only is not advised at present. Some illustrative cases are recorded.

T. N. MacGregor

525. A Review of the Vaginal Smear Method for Early Diagnosis of Cancer. (Report of Cases.)
By G. W. McCLURE. *W. Virginia med. J.*, 43, 66–71, Feb. 1947. 8 refs.

526. Uterine Chorionepithelioma with Severe Intra-peritoneal Haemorrhage.
By C. V. SALISBURY, and B. C. GLASGOW. *Med. J. Austral.*, 1, 334-336, Mar. 15, 1947. 1 fig., 10 refs.

527. Corpus Carcinoma. A Study of Three Hundred and Twenty-two Cases.
By N. F. MILLER and C. W. HENDERSON. *Amer. J. Obstet. Gynec*, 52, 894–903, Dec. 1946. 9 refs.

The authors, impressed by the comparatively poor long-term results following total hysterectomy with removal of Fallopian tubes and ovaries in carcinoma of the corpus uteri, have, for the past 14 years, been using a combination of pre-operative

irradiation either by X-rays or radium, followed by panhysterectomy 6 weeks later. They now favour pre-operative X-ray irradiation, and the results achieved by this combination in 96 cases were as follows: 84.7 per cent of patients survived for 3 years; 77 per cent for 5 years; and 65 per cent for 10 years. The uterus, Fallopian tubes, and ovaries are carefully examined histologically after removal; 15 specimens (15.6 per cent) revealed no carcinoma. From this extensive experience the authors have formed the following impressions: (1) pre-operative X-ray irradiation has proved to be a valuable adjuvant to total hysterectomy and bilateral salpingo-oöphorectomy in the treatment of carcinoma of the corpus uteri; (2) its use clears the uterine infection, reduces uterine size, and decreases pelvic hyperaemia, thereby facilitating operation; (3) pre-operative X-ray irradiation has not in any discernible way interfered with wound healing.

F. J. Browne

528. Radiation Therapy of Uterine Myoma. Critical Analysis of Results in Five Hundred Cases, showing Indications and Limitations.
By R. J. CROSSEN and H. S. CROSSEN. *J. Amer. med. Ass.*, 133, 593–599, Mar. 1, 1947. 3 refs.

A review is made of 549 cases of uterine myoma treated, 90 per cent successfully, during the last 20 years. The authors recommend radiation therapy for certain selected cases of myoma, with undue bleeding in older women. Of the patients, 7 per cent were under 40, 61 per cent between 40 and 50, 30 per cent between 50 and 60, and 2 per cent over 60 years old. The suitable case for irradiation is one where the uterus is the size of a fist or smaller (456 cases in this series with 31 failures). Irradiation was given to 53 tumours of grape-fruit size, with 5 failures, and to 17 cases where the uterus was enlarged almost to the umbilicus, with no failures. Supplementary irradiation was given to 23 of the failures with successful results. The length of time required for success was 6 months in 50 per cent of the cases.

The authors state that when pelvic pain or pressure discomfort is a prominent feature there is little likelihood of a satisfactory result. They believe that there are four necessary steps for the safe handling of the case by radiation therapy: (1) deep pelvic palpation under anaesthesia to exclude ovarian or adnexal disease; (2) curettage to exclude

carcinoma of the uterus; (3) conization of the cervix to remove a source of chronic irritation and possibly to prevent the development later of carcinoma of this area; and (4) accurate recordings of findings at the time of examination.

At the primary examination 23 of the 549 cases were found to have carcinoma of the uterus as well, and a further case had an early carcinoma of the cervix missed at the first examination; 526 cases were therefore treated by the usual radiation dosage (1,200 to 2,400 mg.-hours) to stop myomatous activity and induce an artificial menopause. There were 30 failures. In 6 cases degeneration of the myoma occurred, necessitating operative treatment; in 4 the bleeding continued, as the fibroid was submucous, and hysterectomy was performed; in another 4 cases continuation of bleeding was associated with carcinoma of the endometrium; in 1 there was endometrioma of the uterus; in 2, endometriosis of the adnexa; in 2 carcinoma of the ovary; in 1, simple cyst of the ovary; and in 5 cases chronic salpingitis. Three patients subsequently developed stenosis and pyometra.

The authors claim that 90 per cent success with radiation therapy in 470 patients was obtained with minor risks. The alternative method of treatment would have entailed a major abdominal operation. They further point out the advantage of this treatment in that the patient submits herself at an earlier stage of the disease when she might be inclined to postpone a major surgical operation.

Gladys Dodds

529. The Place of Myomectomy in the Treatment of Myoma Uteri.

By M. S. QURESHI. *J. Obstet. Gynaec., Lahore,* 7, 169–178 and 183–190, Nov. and Dec. 1946. 28 refs.

530. Surgery in the Uterine Fibroid, a Plea for Myomectomy.

By J. W. ROSS. *Amer. J. Obstet. Gynec.,* 53, 266–270, Feb. 1947.

531. Carcinoma of the Cervix.

By W. P. SMITH. *Med. Times, N. Y.,* 74, 32–35, Jan. 1947.

532. Clinico-statistical Notes on Cancer of the Cervix Uteri. (Note clinicostatistiche sul cancro del collo dell' utero.)

By L. CUSMANO. *Ginecologia, Torino,* 12, 249–284, Sept. 1946. 37 refs.

533. Carcinoma of the Cervix During the First Two Decades of Life.

By R. S. POLLACK and H. C. TAYLOR. *Amer. J. Obstet. Gynec.,* 53, 135–141, Jan. 1947. 1 fig., 25 refs.

534. The Effect of Radiation on Vaginal Cells in Cervical Carcinoma. I. Description of Cellular Changes.

By R. M. GRAHAM. *Surg. Gynec. Obstet.,* 84, 153–165, Feb. 1947. 22 figs., 9 refs.

This study comes from the Vincent Memorial Laboratory of the Massachusetts General Hospital, Boston. Vaginal-smear studies were made in 206 cases of cervical carcinoma (27 adenocarcinomata and 179 epidermoid carcinomata) treated by X-rays, radium, or both.

The author first describes the normal vaginal-cell picture and illustrates basal, precornified, and cornified cells and histiocytes. Differentiation or non-differentiation of the malignant cells of epidermoid carcinoma depends on how advanced the tumour is. In adenocarcinoma they are undifferentiated. The cases are divided into four groups: (1) those studied during their radiotherapy; (2) those with a follow-up beginning from 1 to 6 months after treatment; (3) those whose follow-up began at 6 months to 1 year after treatment; and (4) those whose treatment took place 1 to 15 years before the first vaginal smear was taken.

The first group, the 35 cases of cervical carcinoma, fall into 2 classes: (1) those showing definite irradiation in all cells, and (2) those showing very little effect in either normal or malignant cells. The first effect of irradiation is seen in normal cells. The basal cells, by the ninth or tenth day of treatment, lose their round appearance and become elongated while retaining a normal vesicular nucleus: many change their staining reaction from a basophilic to a brownish colour by Papanicolaou's method. Later the nuclei become degenerate. About the twelfth day the cells become greatly increased in size, but the cytoplasmic-nuclear ratio remains constant. About the fifteenth day progressive cytoplasmic vacuolization occurs. Finally the cells become very bizarre in shape. The precornified cells enlarge two to three times in size (fifteenth day), the cytoplasmic-nuclear ratio remaining constant. Their nuclei acquire a dead pyknotic appearance and may become fragmented. The cytoplasm becomes

vacuolated and bizarre, and polymorphonuclear leucocytes become included later in the cells themselves. Similar changes, other than the nuclear ones, occur in the cornified cells. In malignant cells, post-irradiation changes begin usually by the eleventh day. The cells increase in size, their cytoplasm become vacuolated, and they frequently contain several nuclei which appear dead. It is often difficult to say whether an irradiated cell was originally malignant or benign. Nearly half of the cases in this group showed an increase of malignant cells after irradiation had begun. On an average, however, malignant cells have disappeared by the twenty-fourth day after irradiation has begun. Five cases whose treatment was adequate showed little reaction either in malignant or in normal cells.

In the second group, consisting of 50 cases, 18 showed irradiation changes similar to those described above, while 32 did not. In the third group, of 19 cases, 11 showed the expected irradiation reaction, 4 had none, and 4 showed evidence of post-irradiation recurrence of the growth.

The fourth group consisted of 102 cases. If divided by the type of cell found in the smear they fall into three categories. Approximately one-third show only basal cells, one-third precornified cells and basal cells, and the remainder cornified, precornified, and an occasional basal cell. This is not an age difference. Eight showed signs of recurrence.

The author points out that the changes seen in individual cells, both normal and malignant, are comparable to those previously described by workers who have studied biopsy specimens from irradiated patients. Vaginal smear is easier to perform than a biopsy, and can be done much more frequently. Although it does not indicate the depths of the neoplasm, the vaginal smear does show representatives of the entire cell population of the vagina and cervix. Its possible prognostic significance is discussed in a succeeding paper.

Anthony W. Purdie

535. Endometriosis: Diagnosis and Treatment.
By J. RYAN. *Med. Press*, 217, 215–218, Mar. 19, 1947.

536. Endometriosis and Adenomyosis.
By Y. C. YIN. *West. J. Surg.*, 54, 490–493, Dec. 1946. 7 refs.

The terms endometriosis and adenomyosis have often been used synonymously. The author prefers the term adenomyosis for intrauterine aberrant proliferation and endometriosis for extrauterine endometrial conditions. Both are common in Chinese women, most of the patients coming from the upper social class. Endometriosis was commonest between 19 and 32 years, and adenomyosis between 30 and 45 years. Cases of endometriosis outnumbered those of adenomyosis by three to one.

None of the theories so far advanced for the pathogenesis of endometriosis explains all its clinical and pathological manifestations. The conception is gaining ground that excessive ovarian secretion may activate, if not cause, excessive endometrial proliferation. A case is quoted in support of the implantation theory, though it is not claimed that this explains all cases of pelvic and abdominal endometriosis. For adenomyosis it seems likely that a congenital origin, in fact a maldevelopment of the Müllerian ducts, is responsible. Two cases illustrating this are quoted. On the other hand, cases are quoted where, on account of congenital atresia of the vagina, the pelvis was full of tarry, dammed-up blood without any evidence of endometriosis. This is given in support of the idea that excess ovarian secretion is responsible for the activation and maintenance of ectopic endometrial tissue.

The symptoms are briefly described. The belief that adenomyoma is commonly found in retroverted uteri is not substantiated by clinical experience, nor is sterility a diagnostic point.

[The chief interest in this paper, which otherwise contains little that is original, lies in the statement that endometriosis occurs in Chinese women at such an early age. This may be owing to the earlier occurrence of puberty.] *Josephine Barnes*

537. Some Cases of Ovarian Malignancy.
By J. S. QUIN. *Irish. J. med. Sci.*, 121–125, Mar. 1947.

538. Cornification in Ovarian Carcinoma. (Uber Hornbildung in den Ovarialkarzinomen.)
By R. KLEITSMAN. *Acta. obstet. gynec. scand.*, 27, 46–57, 1947. 3 figs., 14 refs.

539. A Case of Sarcoma of the Ovary and of Developmental Anomaly in a 13-year-old Child. (Sopra un caso di sarcoma dell'-ovaio e di anomalia di sviluppo genitale in una bambina di 13 anni.)
By L. U. BARBERIS and U. FONTANA. *Minerva med., Torino*, 38i, 310-313, Mar. 24, 1947. 3 figs.

540. Meigs's Syndrome in Theca-cell Tumor of the Ovary.

By L. E. FRANKENTHAL. *Amer. J. Obstet. Gynec.*, **53**, 331, Feb. 1947.

541. Tubular Adenomas and Testis-like Tubules of the Ovaries of Aged Rats.

By E. T. ENGLE. *Cancer Res.*, **6**, 578–582, Oct. 1946. 5 figs., 4 refs.

A histological examination of the ovaries of aged Wistar rats revealed that a proportion of these ovaries contained tubular adenomata with characteristic epithelial cells showing vague cytoplasmic borders and grooved nuclei closely resembling the Sertoli cells of the seminiferous tubules of rat testis. This type of nucleus has also been found in the Brenner tumour and occasionally in connective tissue, smooth muscle, and ordinary epithelium. Other workers, using the ovaries of a shrew, have demonstrated that the ageing factor in the animal is not dominant. The authors conclude: " The thoughtful suggestion of Robert Meyer that the arrhenoblastomas and other dysgerminomas probably arise from persisting embryonic influences may also apply in these cases of testis-like tubules in the ovaries of aged rats. In these cases, however, the restriction of the tubules to rats in the oldest age groups possibly indicates a type of android proliferation which was permitted only after removal of gynecoid influences."

I. Hieger

542. Pathology and Physiology of Struma Ovarii.

By F. G. SMITH. *Arch. Surg., Chicago*, **53**, 603–626, Dec. 1946. 6 figs., 137 refs.

Ovarian dermoids are often found to contain thyroid tissue if examined in sufficient detail, but the term " struma ovarii " should be confined to ovarian tumours in which thyroid tissue is a major constituent. Such tumours are uncommon. The author tabulates, with brief particulars, the 152 cases recorded in the literature and includes a case of his own. About one-half are examples of dermoids containing, besides thyroid as a major constituent, such tissues as skin, teeth, brain, and intestinal epithelium. One-third are ovarian cystomata, either serous or pseudo-mucinous, containing thyroid. The remaining one-sixth are pure thyroid tumours of the ovary. The author's case belongs to the last and rarest group.

A woman of 58, known for 2½ years to have had a small nodular goitre with mild hyperthyroidism, complained of pelvic discomfort and frequency of micturition. On examination the right lobe of the thyroid was found to contain a firm nodule 2 cm. in diameter, and a round hard mass was felt in the left adnexa. Operation revealed a solid tumour of the left ovary 5 cm. in diameter, the pelvic viscera being otherwise normal. Bilateral salpingo-oöphorectomy was done. Pathological examination of the tumour showed it to be composed of remnants of ovary, normal thyroid tissue, thyroid adenoma, and small foci of osseous formation. The thyroid adenomatous tissue was distributed throughout the tumour in nodules. In places there was evidence of a malignant tendency, the cells showing very active proliferation and invading blood vessels. The patient was alive and well 6 years later.

Close study of the reported cases has brought out the following points. Ovarian strumata occur at all ages, though they are exceedingly rare before 25. An associated cervical goitre is not uncommonly present. Metastases, which may be highly malignant, occur occasionally, local peritoneal implants, and spread to the liver and the bones having all been recorded. Microscopically the appearance of malignancy is often seen. However, it is pointed out that the histological criteria of thyroid malignancy are difficult to formulate, and that it is sometimes held that invasion of the blood vessels is the only reliable distinction between benign and malignant adenomata. The author's case showed this invasion, but metastasis had not occurred. The significance of foci of calcification and ossification, which have often been noted and were present in the author's case, is discussed. The conclusion is reached that they are similar to the calcification and ossification frequently seen in cervical goitres and that their presence is not itself evidence of a teratomatous tumour process. Notwithstanding this the author is of opinion that all ovarian strumata are in fact of teratomatous origin. About 10 per cent of the cases have had thyrotoxic symptoms, and removal of the ovarian struma has led to improvement in a few. This did not occur in the author's patient, whose basal metabolic rate, known to be +19 per cent 2½ years before the operation, remained at about this level afterwards, no doubt because of the coexistent nodular goitre.

[This is a clear and very comprehensive study of

a small subject. There is a complete bibliography. The photomicrographs are of exceptional quality.]

H. J. Croot

543. Solid Teratomas of the Ovary with Neurological Metastases.

By G. G. PROSKAUER. *Amer. J. Obstet. Gynec.*, 52, 845–849, Nov. 1946. 3 figs., 20 refs.

Only 10 cases of peritoneal implantation of nervous tissue derived from an ovarian teratoma have been reported. The rarity of the condition is the reason for reporting this additional case of neuroglial metastasizing ovarian teratoma. The patient, aged 22, had a 4-months history of abdominal pain and swelling. Colostrum was present in both breasts, the Aschheim-Zondek reaction was negative, and there was considerable ascites. Two ovarian tumours were found; that on the left side was a simple dermoid cyst; but the tumour of the right ovary, a good deal larger, was shown to be a teratoma, of which about one-sixth consisted of fat tissue and the remainder mainly of nervous tissue, with here and there islands of hyaline cartilage, mucous glands, sebaceous glands, and hairs. The greater part of the tumour was composed of neuroglia, in some regions having gyrus-like structure. Here and there ganglion cells were found, mature in appearance and with nuclei, nucleoli, axons, and dendrites. No myelin sheaths were seen. In the upper pole of the tumour a completely developed cerebellar cortex was found, having the normal appearance of an internal granular layer, a single layer of Purkinje cells, and an external grey substance. Secondary (implantation) growths were scattered through the greater omentum, which was adherent to the right ovary. These nodules contained neuroglia but neither ganglion cells nor neuro-epithelium. Fifteen months after post-operative X-ray treatment the patient was in good condition.

T. C. Clare

544. Brenner Tumours of the Ovary. (Ueber die Brenners'chen Ovarialtumoren.)

By R. KLEITSMAN. *Acta obstet. gynec. scand.*, 27, 33–45, 1947. 2 figs., 28 refs.

545. Masculinizing Tumours of the Ovary. A Clinicopathologic Survey with Discussion of Histogenesis and Report of Three Cases.

By L. IVERSON. *Surg. Gynec. Obstet.*, 84, 213–238, Feb. 1947. 15 figs., 126 refs.

Much of the previous literature on the subject of virilizing tumours of the ovary is reviewed. Though individual workers differ in their classification of these tumours the consensus is that there are two main types—the arrhenoblastoma and the less common virilizing lipoid-cell tumour. The latter has been given various names, most of which suggest a connection with the adrenal cortex, such as hypernephroma of the ovary and ovarian adrenal rest. The author compares the published data concerning 41 cases recorded as arrhenoblastoma and 24 examples of virilizing lipoid-cell tumour, mostly reported as adrenal tumours of the ovary. The average age of patients (32 years), age distribution (from 15 to over 60), and average duration of symptoms before operation (4 years) were the same in both groups. Amenorrhoea was always present. Virilism, as shown by hirsutism, voice change, breast atrophy, and hypertrophy of the clitoris (not all necessarily in every patient) was invariably found in the cases of virilizing lipoid-cell tumour and in all those of arrhenoblastoma except the most highly differentiated type, usually known as testicular adenoma of the ovary. The only pure examples of this type, 6 in number, showed no virilizing symptoms. Hypertension and diabetic tendencies were found occasionally in both groups; there was nothing to support the view sometimes expressed that they are especially characteristic of the lipoid-cell tumours. The incidence of malignancy was equal, about 10 per cent in both groups. In assessment of prognosis as regards malignancy no help was gained from the histological appearance of the tumour, the least differentiated and most sarcomatous-looking arrhenoblastoma often proving clinically innocent. A rapidly growing tumour, ascites, loss of weight, and return of symptoms after operation were the usual indications of malignancy. The lipoid-cell tumours were smaller and had less tendency to cyst formation. When cut across they showed a characteristic yellowish-orange colour due to intracellular lipoids.

Detailed histological studies were made in the Department of Pathology, Duke University, Durham, N.C., of the tumours from 4 cases, including the 3 here reported. Although the resemblance of the lipoid-cell tumour to adrenal tissue is very striking the author puts forward the view that both types of virilizing tumour are in fact of

true ovarian origin, having a common ancestry from the theca lutein cells. Strong support for this point of view is afforded by one of the author's cases. A large ovarian tumour was removed from a woman of 61 with signs of virilism. The greater part of the tumour was typical of arrhenoblastoma, but a large nodule was present composed of adrenal-like tissue. Further, the only metastasis, a peritoneal implant, contained cells characteristic of both types of tumour.

<div align="right">H. J. Croot</div>

546. Masculinizing Tumor of the Ovary of the Adrenal Type.

By M. DOUGLASS. *Amer. J. Obstet. Gynec.,* 53, 190–198, Feb. 1947. 10 figs., 10 refs.

547. Torsion of a Seminoma of the Ovary. (Séminome tordu de l'ovaire. Intervention d'urgence.)

By M. FATIO. *Mém. Acad. Chir., Paris,* 73, 23–24, Jan. 15 and 22, 1947.

A 48-year-old nullipara was admitted to hospital with a history of vague abdominal and pelvic pain and dysuria. For 3 years she had only menstruated 2 or 3 times a year. Catheterization revealed the presence of 600 ml. of residual urine, and subsequent examination disclosed a large, almost fixed mass to the right of the uterus. Two days later, the patient had a sudden onset of hypogastric pain, and vomited. Palpation of the right iliac fossa and of the right fornix was painful. Immediate laparotomy was performed, and a cyst of the right ovary (of the size of a foetal head) was found to have undergone torsion of its pedicle through 360 degrees. Puncture gave a haemorrhagic liquid. Salpingo-oöphorectomy was performed. Macroscopically, the cyst showed haemorrhagic areas in its wall and an intracystic papilloma of the size of a tangerine. Microscopically, areas with typical structure of a seminoma were found. Estimation of the daily prolan-A excretion in the urine gave a value of 420 rat units. Since it was thought probable that metastases in the lymph nodes were responsible for this finding, X-ray irradiation of the lumbar region was carried out, after which urinary examination for prolan-A became negative.

<div align="right">S. S. B. Gilder</div>

548. Clinical and Pathologic Aspects of Primary Sarcoma of the Uterine Tube.

By L. C. SCHEFFEY, W. R. LANG, and F. B. NUGENT. *Amer. J. Obstet. Gynec.,* 52, 905–916, Dec. 1946. 3 figs., 44 refs.

Primary sarcoma of the Fallopian tube is rare and during the last 60 years only 21 cases have been reported. In the same period 578 tubal caricinomata have been reported, a ratio to tubal sarcoma of about 25 to 1. The authors describe a case of their own. The patient, aged 70, had had 1 pregnancy and was admitted complaining of low pelvic pain with intermittent vaginal discharge, sometimes bloody. The menopause occurred at the age of 55, and 10 months before admission there had been a sudden, rather profuse haemorrhage, for which a diagnostic curettage was done and an intrauterine application was made of radium (1,200 mg. hours). The report on the curettage showed an atrophic endometrium but no malignancy. After this treatment an intermittent bloody *vaginal discharge was noted. Nine months later,* pelvic examination revealed an extremely tender, enlarged, retroflexed uterus with no apparent abnormality in the appendages. A diagnosis of pyometra was made. Vaginal smear (Papanicolaou technique) showed atypical cells suggestive of fundal carcinoma. Laparotomy exposed an atrophic uterus displaced forwards by a more or less fixed swelling in the cul-de-sac, apparently a left pyosalpinx adherent to the uterus. There was no evidence of peritoneal implants and the regional glands were not enlarged. The diagnosis at operation was a left pyosalpinx resulting from radium application. Complete hysterectomy with bilateral salpingo-oöphorectomy was carried out. Recovery was uneventful.

Examination of the removed structures showed that the middle and outer thirds to the left Fallopian tube weer replaced by a grey friable tissue. The fimbrial end was sealed. The inner third of the tube was distended with blood and the wall was very thin. Microscopically the growth was composed of a " very cellular and bizarre growth made up of muscle cells and some fibroblasts "— a myosarcoma of the mixed-cell variety. At the time of writing, 2 years after operation, there is no evidence of recurrence.

The authors discuss the clinical features of the reported cases. The age incidence ranged from 27 to 70. In pre-menopausal patients, menorrhagia or metrorrhagia usually occurred and often, also, an abnormal vaginal discharge, either serosanguineous or semipurulent. In the post-menopausal

groups the discharge was generally bloody but sometimes profuse and watery. In 2 young patients, aged 27 and 37, the menses were normal. In nearly every case pain was a prominent symptom. In no case was the diagnosis made pre-operatively. In 6 cases the tumour was bilateral. The authors emphasize the similarity of the clinical features to those of tubal carcinoma. Vaginal bleeding is not so well marked as in uterine cancer but is more often a watery, blood-stained discharge. Pain is the most constant and con-spicuous symptom and is often associated with gastro-intestinal irritation. Hysterectomy and bilateral salpingo-oöphorectomy is recommended rather than simple removal of the affected tube. The question of post-operative irradiation is undecided and prognosis doubtful.

F. J. Browne

549. Confluent Intertubal Serous Cyst. (Sierocele intertubarico confluente.)

By U. CASABONA. *Ginecologia, Torino,* 13, 1–16, Jan. 1947. 10 figs., 18 refs.

See also No. 410.

Operations

550. Thrombophlebitis and Phlebothrombosis in Gynecologic Patients; the Prophylaxis, Recognition, and Treatment.

By J. V. MEIGS and F. M. INGERSOLL. *Amer. J. Obstet. Gynec.,* 52, 938–945, 959–963, Dec. 1946. 9 refs.

In the surgical wards of the Massachusetts General Hospital, in spite of conservative preventa-tive measures such as the control of posture and the use of exercises, fatal embolism occurred in 1 out of 800 patients undergoing major surgical opera-tions. Because of this danger a means has been sought to prevent embolism after operation, and with that end in view 1,057 ligations of the super-ficial femoral vein have been done in the hospital since 1937. It had been shown by Castleman that nearly all fatal emboli come from the veins of the legs. At present the consensus in the hospital is that failure to ligate at once the veins of a patient who has had a non-fatal pulmonary embolus, or a patient who has definite signs of either thrombo-phlebitis or phlebothrombosis, constitutes serious neglect. In the gynaecological wards in the 5 years 1941–5 there were 3,503 operations and 75 vein

ligations. Death from emboli occurred in 5 cases, in only 1 of which the vein had been interrupted.

The general plan in the hospital is to try to prevent pulmonary embolism by ligation of the appropriate veins in patients who have a suggestion of thrombophlebitis or phlebothrombosis, and to interrupt definitely the femoral veins of those patients who have had a sublethal pulmonary embolus or infarct. Early diagnosis is essential. If any tenderness is found or if the patient com-plains of pain in her legs, the groin, inside of thigh, popliteal space, calf, and veins of foot are pal-pated for tenderness or swelling. The most important sign is tenderness of the calf, which was present in 53 per cent of the 75 patients in whom the veins were ligated. A positive Homans's sign (pain in the calf on dorsiflexion of the foot) is diagnostic but was only present in 28 per cent of the 75 cases. Swelling of the leg is important, while a rise in pulse rate, temperature, and respira-tion rate in addition to other physical findings sug-gests the presence of a small pulmonary infàrct.

Various methods have been tried to prevent venous thrombosis. Early movements, elevation of the foot of the bed, and anticoagulants are being tried out with careful controls. The surgical treat-ment of thrombophlebitis and phlebothrombosis consists in the interruption of the vein above the clot. Both legs must be operated on. A 4-in. (10 cm.) incision is made from the groin downwards along the course of the femoral artery. The sub-cutaneous tissue, superficial fascia, and fascia lata are divided. The femoral pulsation is felt for, and deep to the sartorius muscle and lying on the adductor longus the femoral artery and vein are found. The sheath overlying the vessels is approached from the medial side and the sheath surrounding the vein opened. Inside the sheath the dissection is carried upwards and the superficial femoral vein isolated over a 4-cm. length. Ligatures are placed under it and not tied but held on tension, and the vein opened. Tension is then released when there should be a free flow of blood. If there is not, a suction tube is inserted into the common femoral and suction applied. After the vein is sucked out and a free flow of blood occurs the common femoral and iliac veins are considered to be cleared. The vein is then tied just below the profunda. If the superficial femoral and the pro-

funda are both involved in the thrombosis, it is essential to tie the common femoral vein. " Emboli have followed interruption of the veins, but few have been fatal. . . If emboli do occur they are not fatal, and the use of dicoumarol has prevented further emboli."

F. J. Browne

551. **Phlebothrombosis and Thrombophlebitis in Gynecology and Obstetrics.**
By C. G. COLLINS and E. W. NELSON. *Amer. J. Obstet. Gynec*, 52, 946–963, Dec. 1946. 82 refs.

Intravenous clotting may be associated with two conditions—phlebothrombosis and thrombophlebitis. In the former there is no inflammation, and the clot is loosely attached to the vein wall. Because of this it is liable to break away and give rise to a pulmonary infarct. In thrombophlebitis, on the other hand, the clot is firmly adherent, and, unless suppuration is present, rarely results in pulmonary infarction or embolism.

In phlebothrombosis there is usually little or no swelling, pain, or fever and sometimes pulmonary infarction is the first symptom. Any persistent or undue elevation of pulse rate or temperature should arouse suspicion, and repeated examinations for clinical signs of phlebothrombosis should be made. Examinations of the legs should be a part of the routine care of patients confined to bed. A complaint of pain in the chest or in the lower limbs should not be lightly dismissed. In some cases oedema of the leg is found in phlebothrombosis, especially if the common femoral vein is involved. This is often the case with tumours of the pelvis, in which oedema is apt to be ascribed to pressure by the tumour. Any case of unilateral oedema, and particularly if associated with pregnancy or pelvic tumours, should be considered due to phlebothrombosis of the femoral or pelvic veins until proved otherwise. As to treatment, the " horse and buggy " therapy by elevation of the leg and wrapping it in cotton " batting " is still too often used; it does not prevent pulmonary infarction. Modern treatment consists of either venous ligation or the use of anticoagulants. The authors have had no experience of the latter method.

The diagnosis of thrombophlebitis (phlegmasia alba dolens) is not difficult. Usually fever is present with pain and oedema and tenderness along the course of the vein; if deep veins are involved, especially the femoro-iliac, there is pallor and cyanosis. These symptoms are due not to venous blockage but to reflex vasospasm, resulting in decreased pulsation in the arteries of the limb, increased capillary permeability, and exudation of fluid into the extravascular tissues. Such cases are treated by blocking the sympathetic nerve supply to the involved extremity by procaine hydrochloride. The relief of pain is dramatic, while fever and oedema rapidly subside.

Suppurative thrombophlebitis of the pelvic veins is most often found in cases of puerperal sepsis, though it may follow application of radium, suppurative process in the adnexa, or gynaecological operations. Detachment of the clot sometimes occurs with pulmonary infarction, the suppurative process of the clot causing liquefaction. In one such case after vaginal hysterectomy vena cava ligation was performed; the patient recovered and there were no untoward after-effects. The authors favour ligation of the ovarian vein and inferior vena cava in all cases of suppurative pelvic thrombophlebitis which fail to respond to conservative therapy, including sulphonamides and penicillin. A definite diagnosis of suppurative pelvic thrombophlebitis is fairly difficult to make. " Spiking " fever and chills are often, but not always, present. Occasionally there is a plateau-like temperature curve, and chills may be absent. A fairly constant finding is an elevated pulse rate in a patient who looks less ill than the history and findings would indicate. On vaginal examination little or no exudate is found in the parametrium; sometimes thrombosed veins may be felt there or in the vaginal wall. All lung infarcts do not produce the typical pleural pain and bloody sputum, and they may only be detected by radiographs, though Krause states that " the roentgen diagnosis of pulmonary infarct is probably subject to a greater percentage of error than that of any other lesion of the lung ". Positive blood cultures are of value, especially in determining whether the organism is penicillin-sensitive, but negative ones do not rule out the presence of suppurative pelvic thrombophlebitis. In the authors' series palpable thrombosed vaginal or pelvic veins were found on vaginal examination in only 36 per cent of the cases. No deaths occurred in the ligations following gynaecological operations, but in ligations for puerperal suppurative thrombophlebitis there were 2 deaths (13.5 per cent). In

both cases the ligation was too long delayed in the the hope that penicillin and sulphonamides might effect a cure. No ill-results, such as oedema, seemed to follow the ligation of the inferior vena cava. This freedom from after-effects is, in the authors' opinion, due to the fact that they routinely carried out paralumbar sympathetic block, or, in their later cases, sectioned the right and left sympathetic chains at the time of ligation.

In the discussion that followed this paper and that of Meigs and Ingersoll (see Abstract 549) Curtis condemned venous ligation as an unnecessary procedure. Heparin and dicoumarol therapy he believed to be simpler, safer, and more satisfactory. Masson considered it difficult to decide what veins should be ligated; he said that the "promiscuous ligation of major veins as a prophylactic measure is not warranted, especially in view of the possible sequelae that may be a definite handicap to the patient in future years".

F. J. Browne

532. Investigations on the Uterine Mucosa. I. Biopsy Material, its Treatment and Evaluation. [In English.]

By B. FALCONER. *Acta obstet. gynec. scand.,* **26,** 453–474, 1946. 8 figs., 28 refs.

Investigations on the Uterine Mucosa. II. The Occurrence and Significance of Ectatic and Cystic Glands in the Uterine Mucosa. [In English.]

By B. FALCONER. *Acta obstet. gynec. scand.,* **26,** 475–495, 1946. 2 figs., 12 refs.

Investigations on the Uterine Mucosa. III. On the Early Diagnosis of Metropathia Haemorrhagica. [In English.]

By B. FALCONER. *Acta obstet. gynec. scand.,* **26,** 525–545, 1946. 10 figs., 7 refs.

In this series of articles the author reviews the methods of obtaining biopsy material from the uterus and the methods of examining it. He has used the facilities of the Department of Women's Diseases at Stockholm and the Department of Gynaecology at the Radiumhemmet to obtain specimens.

The characteristic changes in curetted material are fresh haemorrhages, signs of invaginations of the glands, and cadaveric processes of varying degree. The author believes that invagination, being found in the basalis, is not merely an artefact but is partly conditioned by the firm stroma of the basalis or is a sign of glandular hyperplasia.

Modern methods of obtaining strip curettings by suction or cannula are open to many criticisms from the pathologist, however useful they may be to the clinician. As the author puts it: " It would be, of course, unreasonable to judge the quality of the wallpaper of a room by a sample taken offhand." Suction curettage, too, leads to fresh blood extravasations. In a discussion of the various staining techniques the difficulties of assessing the secretory contents of the glands are emphasized.

Ectatic and cystic glands were found in 20 cases during the reproductive period of life. They occur in the presence of hypoplasia, hyperplasia glandularis cystica, endometritis, atrophy, and in the angle between a myoma and the underlying uterine wall. Ten of the patients had definite pathological conditions—myoma 2, endocrine dysfunction 4, hyperplasia 4. The other 10 patients had cysts not associated with such easily explained causes, but 5 were women who had had recurrent miscarriages and 5 were sterile women. The author considers such cysts to be a symptom of ovarian insufficiency.

Finally, the author discusses the early pathological changes found in the cystic hyperplasia of metropathia haemorrhagica. All patients in whom the diagnosis had been made have been followed up and further biopsies obtained. Fluhman's work is accepted as a basis of the histological appearances. The author believes that the characteristics of early hyperplasia are: (1) epithelial: increase in the number of cells, packing together of cells, signs of invagination, dilated and cystic glands, epithelial cells with elongated nuclei; and (2) mesenchymal: hyperplasia confined to well-defined areas, cells of " the prematurely ripe type rich in fibrils, lymphatics, and dilated blood vessels ". Six cases of early glandular hyperplasia are fully described clinically and histologically.

[This series of papers forms most interesting reading and is welcome as the cases are fully followed up. It provides an up-to-date account of the aspects of curetting with which it deals.]

Kenneth Bowes

553. Injuries Caused by Hysterosalpingography. [In English.]

By P. HOLM-NIELSEN. *Acta obstet. gynec. scand.,* **26,** 565–597, 1946. 39 refs.

The author has made an exhaustive study of the complications of lipiodol insufflation of the

Fallopian tubes. The literature is first reviewed in detail, and then an analysis of replies to a questionary (covering about 12,000 cases) sent to all Danish hospitals is described. Finally, 1,100 operations during the last 4½ years at the Aarhus Municipal Hospital are investigated. The most frequent complications are inflammatory (0.25 per cent), and these usually consist of a·recurrence of previous infection. The iodized oil is not considered to be incriminated. When at a later date laparotomy has followed lipiodol insufflation, minor adhesions have been found in the pelvis with small granulomatous areas on the peritoneum. These changes are not important. " Iodism " has not been met with in any case. There were only 5 cases of oil embolism and in none did the patient suffer discomfort. No proof was found that tubal pregnancy was likely to follow the operation.

The author concludes that although hysterosalpingography is a minor operation its performance entails definite risks, but that these are far outweighed by its usefulness both in diagnosis and in treatment.

Braithwaite Rickford

554. Oil · Embolism Following Hysterosalpingography.

By F. M. INGERSOLL and L. L. ROBBINS. *Amer. J. Obstet. Gynec,,* 53, 307–311, Feb. 1947. 3 figs., 9 refs.

555. Uterosalpingography. Report of a Fatality.

By A. M. FARIS and A. McMURREY. *Tex. St. J. Med.,* 42, 592–597, Feb. 1947. 9 figs., 13 refs.

556. Surgery of Perforation of the Uterus with Severe Intestinal Lesions. (Sulla chirurgia delle perforazioni dell'utero con gravi lesioni intestinali.)

By A. BILLI. *Clin. ostet. ginec.,* 49, 30–35, Jan.-Feb., 1947. 3 figs.

557. Plastic Operations in Hysterectomy.

By O. S. COFER. *Sth. med. J.,* 40, 31–36, Jan. 1947. 8 figs., 5 refs.

One hundred cases of vaginal hysterectomy, in all of which an anterior colporrhaphy, a perineorrhaphy, and in some instances additional plastic operations for control of urinary incontinence, rectocele, or cystocele, were performed more than 5 years previously, are compared with 100 cases in which similar operations have been performed in the last 5 years. The cases are selected and not consecutive. Though the different time factor in

the two series will invalidate some comparisons, shortening of the vagina, which was particularly common in the first group, is unaffected by time. The comparative table below indicates the results obtained.

	Over 5 years	Under 5 years
Shortened vagina	25	3
Stress incontinence before operation	36	42
Relieved by Kelly operation ...	24	40
Stress incontinence after operation (not present before)	8	0
Vaginal-vault prolapse recurrence, with cystocele and rectocele ...	16	2
Total cases	100	100

The author's operative technique is explained in detail. This largely follows the modifications of Mayo or of Goffe and Ward, and particular attention is paid to the shaping of the epithelial flaps of the vagina to be removed in order to lengthen both the anterior and posterior vaginal walls. The author believes in fixing the bladder neck vaginally to relieve stress incontinence by using the method of Kennedy and Counseller. [This involves mobilizing the urethra, and must subsequently give rise to increased fibrosis and fixation.]

D. M. Stern

558. Bacteriology of Vagina in Total Hysterectomy.

By C. J. DUNCAN. *Amer. J. Obstet. Gynec.,* 53, 324–325, Feb. 1947.

559. Frequency of Carcinoma in a Residual Cervical Stump and Mortality from Total Hysterectomy as Compared with that from Subtotal Hysterectomy. (Frequenza del carcinoma sul moncone residuo e mortalità dell'isterectomia totale nei confronti dell subtotale.)

By C. CANTONE. *Ginecologia, Torino,* 12, 285–295, Sept. 1946.

560. An Operative Procedure for the Repair of the Urethrodiverticulovaginal Fistula. Report of Two Cases.

By W. W. SCOTT and W. L. EKAS. *Surgery,* 20, 645–655, Nov. 1946. 10 figs., 3 refs.

The authors describe in detail the clinical findings and operative technique in 2 cases of this very rare condition, which they call urethro-diverticulovaginal fistula. In a review of the literature they

could find only 2 other cases described. The condition is acquired. The patients complain of frequency and urgency of micturition, dysuria, and urinary obstruction in varying degree. As the fistula leads also to urinary incontinence, it is important that it should be remembered when vesico-vaginal or uretero-vaginal fistula has been excluded. The article explains by means of diagrams the operative technique of repair.

[The urologist and the gynaecologist will be interested to read of this condition, particularly at this time, when more interest is being evinced in the anatomy, physiology, and pathology of the female urethra.]

G. Gordon Lennon

561. The Artificial Autotransplantation of Endometrium in Supra-vaginal Amputation of Uterine Myoma.
By R. BUDIMLICH. *Srpski Arkhiv.,* 45, 21–25, Jan. 1947.

562. A Modification of the Plastic Operation on the Pyramidalis Fascia in Urinary Incontinence. Operation by the Abdominal Route only. Report on Three Cases. [In English.]
By A. SJÖVALL. *Acta obstet. gynec. scand.,* 26, 546–554, 1946. 5 refs.

Three cases of stress incontinence treated by Sunde's modification of the Goebel-Stoeckel operation are described. A single fascial strip 4 cm. wide is taken in the midline from the umbilicus to the pyramidalis (if present). This length of fascia is drawn beneath the bladder neck and sutured to its origin near the symphysis pubis. Damage to the urethra is avoided by injecting 4 ml. of local anaesthetic solution between the anterior vaginal wall and the urethra. Also a finger is kept in the vagina to palpate the passage of the forceps as it is passed from above beneath the urethra. All the cases made good progress, and the symptoms remained cured during the period of a short follow-up. Stress is laid upon the avoidance of infection of the prevesical cellular tissue, and therefore of sloughing the fascia, by using the single abdominal incision and not opening the infected anterior vaginal wall.

[Fascial sling operations such as the Millin sling and Aldridge operation are very popular at the moment. The author states that the indications for the operation are: (1) failure of a previous anterior

colporrhaphy and suburethral repair; and (2) virginity or multiparity of the patient. A third type of patient for whom the operation is indicated might be added—the chronic bronchitic who is rarely if ever free from cough. The risks of infection from a vaginal incision have been overrated and would seem to be less than those of urethral damage.]

Braithwaite Rickford

563. Suprapubic Transvesical Repair of Vesico-vaginal Fistula.
By R. F. SHARP and M. M. GREEN. *Urol. cutan. Rev.,* 50, 632–636, Oct. 1946. 3 figs., 10 refs.

There are three methods of approach in the treatment of vesicovaginal fistula—namely, vaginal, transperitoneal, and transvesical. There are certain indications for the suprapubic transvesical approach. The bladder must be carefully examined by cystoscopy and the size, location, and number of openings must be accurately determined. The indications are listed as follows: (1) A fistula high in the vaginal vault, especially after a total hysterectomy where no cervix remains and the operator therefore cannot pull the operative field downwards and facilitate the vaginal exposure. (2) A contracted and narrow vaginal vault. (3) In the presence of a uretero-vaginal fistula. (4) A fistula close to a ureteric orifice which might be included in a blind vaginal approach. (5) Where stones, polypi, or aberrant bands of tissue in the bladder require surgical treatment. (6) Where the opening to the bladder communicates with the cervical canal. (7) Where a vaginal operation has failed.

As the operation is one of election the patient's general condition must, if necessary, be built up before operation. The authors prefer spinal analgesia. A toilet is done of the vagina and a large gauze roll is inserted, one end being left out so that it may easily be withdrawn by a non-sterile operating-room assistant. The purpose of this pack is to elevate the bladder and make the operation field more accessible. A sub-umbilical midline incision is made, and the bladder exposed and opened widely. If the opening of the fistula is near a ureteric orifice a catheter is passed along the ureter. The tract is completely excised by means of a circular incision approximately 2 mm. from its margin. A line of cleavage is then developed

between the bladder and the vaginal walls: this is probably the most difficult part of the operation. It may be necessary to make a sagittal incision through the whole detrusor portion of the bladder in order to obtain sufficient mobility of the floor to close the opening without tension. The vagina and bladder are closed in layers, No. oo chromic interrupted sutures being used. The anterior incision in the bladder wall is closed around a large de Pezzer catheter.

A. W. Badenoch

See also Nos. 443, 487, 488, 499, 501, 502, 529, 530.

Miscellaneous.

564. Hernia of the Internal Female Genitalia. (Sulle ernie dei genitali interni femminili.)
By P. ALFIERI. *Clin. ostet. ginec.*, **49**, 22–29, Jan.–Feb. 1947. 2 figs., 34 refs.

565. Peritoneal Uterine Fissure due to Spontaneous Rupture of Subserous Vessels in General Fragility of the Veins. (Fissura uteri peritonealis durch Spontanruptur subseröser Gefässe bei allgemeiner Venenschwäche.)
By H. K. v. RECHENBERG. *Schweiz. med. Wchsr.*, **77**, 357–359, Mar. 22, 1947. 9 refs.

566. Vesicovaginal Fistulae.
By I. YOVANOVICH and D. YEREMICH.
Srpski Arkhiv., **45**, 25–31, Jan., 1947. 7 refs.

567. Spontaneous Closure of Post-irradiation Vesicovaginal Fistula. Case Report.
By G. C. MILNOR. *Proc. Clin., Honolulu*, **12**, 207–208, Dec. 1946.

568. 540 Cases of Genital Prolapse Observed at the Gynaecological Clinic of the School of Medicine. University of Bahia (1911-1946). (Revisao de 540 casos de prolapso genital observados na clínica gine-cológica da faculdade de medicina de Bahia, desde a sua criação até hoje [1911–1946].)
By A. PELTIER DE QUEIROZ. *An. brasil, Ginecol.*, **22**, 435–452, Dec. 1946. 7 figs., 5 refs.

569. Chronic Uterine Inversion. (Inversión uterina crónica.)
By H. CABRERA. *Bol. Soc. chil. Obstet. Ginec.*, **11**, 183–185, Oct. 1946. 5 refs.

570. Massive Intraperitoneal Hemorrhage Caused by Rupture of Hemorrhagic Corpus Luteum.
By E. B. PEDLOW. *Ohio St. med. J.*, **43**, 168-169, Feb. 1947. 1 fig., 1 ref.

571. Leucoplakia Vulvae. Its Etiology and Results of Treatment with Vitamin A. Preliminary Report.
By M. N. HYAMS and O. H. BLOOM. *Amer. J. Obstet Gynec.*, **53**, 214-220, Feb. 1947. 6 figs., 4 refs.

The authors investigated a group of 18 patients at New York Post-Graduate Hospital in all of whom the diagnosis of leucoplakia vulvae had been verified by histological examination. The only significant finding was that 60 per cent of the cases had little or no hydrochloric acid in the gastric contents. As anacidity and subacidity of the gastric contents are associated with low plasma content of vitamin A, the authors treated the patients with 250,000 to 500,000 units daily by mouth, supplemented by twice-weekly injections of 50,000 units. In addition each patient was given 15 minims of dilute hydrochloric acid in water three times daily. Fourteen patients improved objectively and subjectively. In the other cases, which were unimproved, there was in addition some constitutional disease—diabetes (2), syphilis (1), and cardio-renal vascular lesion (1).

Gladys Dodds

Foetal and Neonatal Mortality*

BY

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This paper concerns itself with the mortality of all the foetuses which have reached at least the period of viability. By a "viable foetus" I mean one that shows 2 or all of the following 3 criteria: (1) The length of gestation is at least 28 weeks. (2) The weight of the foetus is at least 1,000 g. (2.2 pounds). (3) The length of the foetus is a least 35 cm. (14 inches). By "neonatal death" is meant the death of a baby born alive but dying before its mother has left the hospital or within the first month of life if delivery took place at home.

Table I shows the death-rates of infants and viable foetuses (exclusive of stillbirths) in 34 countries. These statistics (U.S. Department of Commerce, 1946a) reveal that the loss of life early in extrauterine existence is extremely high but not as great as is that during intrauterine existence. Yerushalmy (1945) states that "By conservative estimate 1,225 conceptions are necessary to produce 1,000 infants surviving their first year of life. Of the 225 wasted pregnancies, about 150 terminate in abor-

tion (at least one half of which are induced), at least 30 result in stillbirths and the other 45 infants are born alive but die before their first birthday (infant mortality)". The statistics listed not only do not take into consideration stillbirths but also abortions and ectopic pregnancies, yet in order to obtain a true picture of the actual early loss of human life thése two groups must be considered instead of only "deaths per 1,000 live births." In 1944 in the United States the infant mortality rate was 39.8 per 1,000 live births but in addition to this the stillbirth rate was 27.0 per 1,000 live births. The actual number of stillbirths in the United States in 1944 was 75,495 (U.S. Department of Commerce, 1946b). The number of abortions and ectopic gestations is unknown.

A high death rate is associated with the sudden change from intrauterine to extrauterine existence; it is considerably higher than that of any other day of life. For example, during 1944, in the United States 111,127 babies, exclusive of stillbirths, died in the first year of life. Of these 111,127 deaths 29 per cent were infants less than 1 day old and 60 per cent were less than 1 month old. In spite of the fact that the total infant mortality declined from 71.7

per 1,000 live births in 1925 to 39.8 in 1944, the proportion of neonatal deaths to total infant deaths increased from 52.7 per cent for 1925 to 62.1 per cent for 1944. The increase in the proportion of deaths of infants less than 1 day of age is even more pronounced for this period. These deaths accounted for 20.9 per cent of the total infant mortality in 1925 and 28.8 per cent for 1944. This unfortunate fact is true for most countries. We know that the first 15 minutes after birth is the most dangerous period of life.

Can this frightful waste of human lives be curtailed? I believe the answer is a decided affirmative.

Table I shows that in many countries there has been a considerable decrease in the infant death-rate from 1930 to 1944. Yerushalmy (1945) has calculated that between World Wars I and II, the four belligerent countries in Europe—Germany, France, England and Italy—saved, through a reduction in infant mortality alone, some 3,750,000 of lives or 80 per cent of the more than 4,600,000 military casualties of these four countries killed during the four years of World War I.

As obstetricians we are concerned with the deaths which occur during the first 4 weeks of life but particularly with those which take place on the first day. The purpose of this paper is to attempt to point out how the foetal and neonatal death-rates may be reduced considerably. Before we can find the remedies we must know the causes. The only certain way to determine the cause of death in most instances is to perform autopsies on all dead-born foetuses and also on all the babies who die after delivery. Because the incidence of post-mortem examinations is not as high as it should be, the collected statistics from different cities and countries do not give accurate information concerning the causes of foetal and infant deaths. However, two

TABLE I.

Infant Mortality per 1,000 Live Births in 34 Countries, 1930–1934 (exclusive of Stillbirths)§

Country	1930	1935	1940	1944
Argentina ...	106	107	90	78†
Australia ...	47	40	38	31
Austria	104	98	72	78†
Belgium ...	93	77	85	77
Brazil	184	204	180	191
Canada ...	89	71	56	55
Chile	234	251	217	181
Denmark ...	80	71	50	48
Eire	66	68	66	79
Egypt	151	161	162	—
England and Wales	60	57	56	45
Finland	75	67	88	—
France	78	69	92	77
Germany	85	69	63	—
Greece	99	113	—	—
Hungary	153	152	130	—
India, British ...	181	163	160	—
Italy	106	101	103	—
Japan (proper)	127	107	—	—
Mexico	132	126	126	114
Netherlands ...	51	40	39	41†
New Zealand ...	34	32	30	30
Northern Ireland	68	86	86	67
Norway	46	44	39	—
Palestine	154	131	127	87
Poland	142	127	—	137†
Portugal	144	149	126	122
Scotland	83	77	78	65
Spain	117	109	109	99†
Sweden	55	46	39	30
Switzerland ...	51	48	46	42
Union of South Africa	67	63	50	42
United States ...	65	56	47	40
Uruguay	100	102	86	—

§ The data are not always all inclusive.
† This figure is for 1943.

reports from Great Britain are conspicuous exceptions. In 1926 Holland and Lane-Claypon published the data of the autopsies and clinical histories of 1,673 dead-births and neonatal deaths. The authors state: "The data set out in this report do not readily lend themselves to a concise summary." However in Table II, which is reproduced from Holland and Lane-Claypon's monograph, an excellent summary of the causes of death of the 1,673 babies born in London, Glasgow, Liverpool, Edinburgh and Cardiff is given.

TABLE II.

Showing Percentages of Deaths Assignable to the Various Causes

Cause			London	Glasgow	Liverpool	Edinburgh	Cardiff
Complication of Labour	...	...	34.8	40.2	31.2	37.2	30.2
Antepartum haemorrhage	...	...	21.7	30.7	14.3	10.5	17.0
Toxaemia of pregnancy	...	...	12.7	10.7	7.7	10.2	20.1
Syphilis	...	...	7.7	7.0	8.6	11.1	8.5
Maternal states	...	...	5.9	2.5	2.0	1.5	0.8
Placental states	...	...	0.9	0.0	2.0	1.7	1.5
Foetal states ...	...	...	5.0	5.4	23.6	7.2	10.8
Prematurity	...	...	0.0	0.3	2.0	10.4	3.1
Cause unknown	...	...	11.3	3.2	8.6	10.2	8.0

The other British report was published by Cruickshank in 1930 and is based on autopsies of 800 babies dying neonatally. In 540 or 67.5 per cent of the 800 cases the causes of death were asphyxia neonatorum, congenital atelectasis, prematurity or birth injury; that is, conditions associated with delivery. Of these 540 infants 140 were mature and 400 were premature; 244 or 45.2 per cent of the 540 infants lived less than one day. In 238 or 29.75 per cent death was the result of some infective condition; the infection being acquired either before, during or after delivery. In 22 cases or 2.75 per cent the cause of death was developmental defects and anomalies of such a nature or degree as to be incompatible with survival. Syphilis was responsible for less than 1 per cent of the deaths.

I should like to present statistics from 3 large institutions in the United States. At the Chicago Lying-in Hospital, which was founded by the late Joseph B. DeLee, autopsies have been performed on 81 per cent of all infants and foetuses who failed to survive. In recent years the incidence of autopsies has risen to 95 per cent. For this reason I present the statistics of the Chicago Lying-in Hospital as reported by Potter and Adair (1943).

From the opening of the new Chicago Lying-in Hospital in 1931 until 1941, 27,321 infants were born in the institution.

The total reportable mortality, which includes all liveborn and stillborn infants advanced to the 5th month of gestation, was 4.28 per cent. Of the 1,173 infants 614 were born dead and 559 were born alive but died before leaving the hospital. Slightly less than one half of the foetuses and infants weighed less than 1,500 g. (3.3 pounds). It was possible to find evidence of the probable cause of death in more than 90 per cent of term infants who died during labour or after birth. In the entire series of 954 autopsies, demonstrable abnormalities were present in 64 per cent (maceration was not considered a pathological change). In Table III these lesions are listed.

TABLE III.

Pathologic Lesions Demonstrated in 954 Autopsies Performed at the Chicago Lying-in Hospital

Lesion				Number	Per cent
Anoxia	...	...		242	25.4
Traumatic haemorrhage	...			130	13.6
Malformations	...	...		130	13.6
Pneumonia ...	...	...		55	5.8
Blood dyscrasia	...	...		29	3.0
Syphilis	...	...		2	0.2
Miscellaneous	...	...		20	2.0
No abnormalities	...	...		346	36.4
Total ...	...	...		954	100.0

Anoxia, which was responsible for the highest percentage of deaths (25.4 per cent), was most common when *death* occurred during labour, and it was found

with almost equal frequency in premature and in mature infants. The diagnosis was based on the presence of discrete petechial haemorrhages in the lungs or thymus and/or petechial haemorrhages in the brain substance. Whereas the incidence of anoxia is given as 25.4 per cent it was actually present in almost 40 per cent because it was a complicating factor in infants who died of traumatic haemorrhage, malformations and other causes. The chief obstetric complications, associated with anoxia, were abruptio placentae, placenta praevia and prolapse or entanglement of the cord.

Traumatic haemorrhage was the cause of death in 13.6 per cent of the cases and 114 of the 130 haemorrhages were intracranial. Major malformations were as frequent as fatal traumatic haemorrhages. If the frequency of malformation is the same among the 20 per cent of infants and foetuses who were not examined at autopsy as among those who were, the incidence of malformation as a primary cause of death is one in every 170 births.

Pneumonia was the primary cause of death in 5.8 per cent of all foetuses and infants. Blood dyscrasia was the cause of death in only 3 per cent. There were only 4 fatal cases of true haemorrhagic disease of the newborn among the 27,321 babies, an incidence of one in 7,000. The remaining 26 babies with blood dyscrasia had erythroblastosis. There were only 6 infants who showed syphilis at autopsy and in only 2 of these was the disease believed to be the primary cause of death. Almost two-thirds of the babies who showed a pathological lesion at autopsy were premature.

In analyzing the time of death, Potter and Adair (1943) found that 32 per cent occurred before the onset of labour, 21 per cent during labour or delivery and 47 per cent after birth. Among the 372 foetuses which died prior to the onset of labour almost one half were macerated. In more than half of the deaths before the onset of labour known environmental conditions were present which may have contributed to the fatal outcome. The majority of these consisted of disturbances preventing a normal exchange of metabolites between the foetal and maternal circulation. They were present in 33 per cent and include abruptio placentae (63 cases), placenta praevia (16 cases), cord prolapse and entanglement (27 cases), maternal shock (3 cases), and miscellaneous conditions (18 cases). Maternal toxaemia was present in 17 per cent.

Only 22 per cent of the 242 foetuses who died during labour or delivery failed to show pathological lesions in contrast to 58 per cent of those dying in the antepartum period. The most common findings were first, anoxia; second, malformation; and third, intracranial haemorrhage. The most common maternal complications, associated with 26 per cent of all antepartum deaths were placenta praevia and abruptio placentae. Toxaemia was present in 13 per cent of all these mothers.

The 559 neonatal deaths make up almost half of the combined infant and foetal mortality. Although only 5.4 per cent of all babies delivered alive at the Chicago Lying-in Hospital were viable prematures, this group accounts for 48 per cent of the deaths. The previable infants make up an additional 16 per cent of the total mortality. The mortality rate for viable, premature infants (weighing 1,000 to 1,500 g. or 2.2 to 3.3 pounds), born alive in this institution, is 19 per cent and for mature infants it is 0.7 per cent. The neonatal mortality for viable premature infants is thus 27 times that of mature infants. Seventy per cent of the 559 infants who died after birth lived less than 24 hours. As previously stated this incidence was 29 per cent for the entire United States in 1944.

At autopsy on 450 infants dying after

birth, the most common abnormality was intracranial haemorrhage with evidence of anoxia occurring almost as frequently. Malformations were third in frequency. The most common maternal complications in this group, like those in the stillborn group, were conditions leading to interference with intrauterine circulation. They were associated with 20 per cent of the deaths occurring after birth and include placenta praevia (49 cases), abruptio placentae (37 cases) and cord prolapse or

babies examined at autopsy. The death rate of 5.3 per cent for Caesarean section is high but 67 per cent of the babies were premature. The chief causes of death at autopsy of the babies delivered by Caesarean section were anoxia, first, and prematurity, second.

Two-thirds of the babies who died following mid or high forceps deliveries and were examined at autopsy showed intracranial haemorrhage; this was the highest incidence of any group. The high percentage

TABLE IV.
Foetal Mortality in Relation to Method of Delivery. *

Method of delivery	I Total hospital deliveries	II Total deaths		III Deaths possibly related to method of delivery		IV Percentage of prematures in Column III
		No. of deaths	Percentage of total deliveries	No. of deaths	Percentage of total deliveries	
Natural cephalic	16440	498	3.1	191	1.1	63.3
Low forceps	6832	100	1.5	74	1.1	27.0
Mid and high forceps ...	1133	59	5.2	48	4.3	12.5
Version and extraction ,	246	72	29.3	49	22.0	51.0
Breech	1050	208	19.8	86	9.3	61.6
Caesarean section ...	1462	127	8.7	76	5.3	67.1
Other	158	109	69.0	37	40.3	56.7

ᵃ Excluded are antepartum deaths and deaths of previable, malformed erythroblastotic and syphilitic infants.

entanglement (26 cases). Maternal toxaemia was associated with 14 per cent of all postnatal deaths.

Table IV (from Potter and Adair, 1943) shows the foetal mortality in relation to the method of delivery at the Chicago Lying-in Hospital. This table is self-explanatory but a few points are worth emphasis. Spontaneous cephalic delivery and delivery by low forceps were associated with the same proportionate number of deaths (column III). The mortality following breech delivery was 8 times that of natural cephalic delivery. Intracranial haemorrhage was the principal pathological cause. It occurred in 43.4 per cent of the breech

of death (22 per cent) in the version and extraction group may be explained by the fact that, at the Chicago Lying-in Hospital, except for the delivery of a second twin, this operation is rarely used unless a maternal or foetal indication for immediate delivery exists. This means that the life of the foetus is usually greatly threatened before the operation is performed.

It was found by Potter and Adair (1943) that both stillbirths and neonatal deaths rise constantly in direct relation to advancing maternal age. There is a striking rise in antepartum and intrapartum foetal deaths between ages 40 and 44 years. This rise was observed for all causes except mal-

formations. The incidence of malforma-tion remained practically constant until 40 years of age, then it doubled between 40 and 44 years.

Other institutions in the United States in which a high autopsy-rate obtains are the New York Lying-in Hospital and the Sloane Hospital for Women. In these two hospitals D'Esopo and Marchetti (1942)

TABLE V.
Cause of Infant and Foetal Death.

Cause of death	New York Lying-in Hospital and Sloan Hospital for Women, per cent	Chicago Lying-in Hospital, per cent
Anoxia	19.8	28.7
Primary prematurity ...	18.5	14.4
Congenital malformation	14.1	11.1
Birth trauma	11.6	13.0
Infections	8.1	4.7
Erythroblastosis	2.8	2.2
Haemorrhagic disease	2.1	0.3
Syphilis	0.6	0.2
Maceration and maternal toxaemia	5.2	5.3
Maceration, no toxaemia	13.5	11.9
Unknown, not macerated	3.0	6.5
Miscellaneous	0.7	1.7
Total mortality	3.87	4.28
Mortality over 1,000 g.	3.52	3.50
Total cases	1000	1173
Stillbirths		614
Deaths		559
Duration of study, 1935-1940		1931-1941

found that among 25,823 deliveries there were 1,000 foetal and neonatal deaths, an incidence of 3.87 per cent. The incidence of autopsies in this group was 89.3 per cent. The causes of death are listed in Table V which was prepared by Potter (1944) to compare the percentages in the New York series with those of the Chicago Lying-in Hospital.

In 11.8 per cent of the New York cases, the foetal deaths were the direct or indirect result of maternal disease. In labour that

TABLE VI.
Relationship of Foetal and Neonatal Mortality to Method of Delivery.

Method of delivery	Total delivered	Total deaths	Percentage rate
Spontaneous vertex	19916	529	2.6
Low forceps	2672	89	3.3
Midforceps	1011	65	6.4
Caesarean section ...	782	57	7.3
Breech delivery ...	1084	152	14.0
Version, extraction	182	42	23.1
High forceps ...	29	12	41.4
Craniotomy	38	38	100.0
Miscellaneous ...	—	16	—

exceeded 30 hours the foetal mortality-rate was doubled. Women more than 30 years of age had a disproportionately greater number of dead babies than did women less than 30. Table VI (D'Esopo and Marchetti, 1942) shows the death-rate according to the method of delivery.

This table like Table IV shows that the least number of deaths occurred after spontaneous vertex and low forceps deliveries. The mortality for breech deliveries was almost 5 times that for spontaneous deliveries. The death-rate for babies

TABLE VII.
Final Diagnosis of Cause of Death of 2000 Foetuses and Infants Based on Clinical and Anatomic Evidence.

Cause	Number	Per cent
Prematurity	416	20.7
Asphyxia	324	16.1
Birth trauma	255	12.7
Malformations	209	10.4
Pneumonia	132	6.5
Erythroblastosis	39	1.8
Syphilis	26	1.2
Miscellaneous	22	1.1
Maternal toxaemia without other cause	97	4.7
Unknown:		
1. Premature	231	12.5
2. Term	249	12.3
Total	2000	100 0

1. Antepartum deaths before term.
2. Includes 145 antepartum deaths at term.

delivered by Caesarean section was almost 3 times that for spontaneous delivery but many of these babies were premature or had congenital anomalies. However 5 of the 57 babies delivered by Caesarean section died of a birth-injury.

Potter (1940) analyzed a series of 2,000 autopsies performed on foetuses and infants which died in the city of Chicago.

TABLE VIII.

Foetal and Neonatal Deaths at the Chicago Lying-in Hospital from July 1st, 1944 to July 1st, 1946.

Total births—6,954.
Total deaths—197 or 2.8 per cent.

	Still-births	Neonatal deaths	Rate per 1,000 births
(1) Malformations ...	8	18	3.7
(2) Erythroblastosis ...	6	13	2.7
(3) Anoxia	15	0	2.1
(4) Pneumonia	0	10	1.4
(5) Birth trauma ...	1	7	1.2
(6) Meningeal oedema	0	7	1.0
(7) Syphilis	1	0	0.1
(8) No pathological lesions found at autopsy :			
(a) Term (over 2,500 g.) ...	18 (14)	7	3.6
(b) Premature (1,000 to 2,500 g.) ...	24 (23)	11	5.0
(c) Previable (400 to 1,000 g.) ...	20 (17)	31	7.3
Total	93 (54)	104	28.1

(Numbers in parentheses are antepartum deaths.)

Deaths occurred antepartum in 39.75 per cent. The causes of death are listed in Table VII.

Dr. Edith L. Potter prepared Table VIII for me from the most recent statistics of the Chicago Lying-in Hospital. We observe that malformations constitute the most frequent cause of death; erythroblastosis is second; anoxia, third; pneumonia, fourth; and that birth trauma is fifth. However the total number of cases studied was relatively small.

DISCUSSION.

What can we learn from these valuable statistics ? First that there is a large waste of human lives before, during and shortly after birth. Second that we can and therefore should reduce the number of foetal and neonatal deaths.

In the present state of our knowledge many of the foetal and infant deaths are definitely not preventable. We have no way as yet of preventing monstrosities and this group constitutes more than 10 per cent of all such deaths. However, there are three ways in which a slight reduction can be made in the frequency of monsters : (1) Since a woman who has given birth to a deformed baby has a greater chance of having more abnormal babies the incidence of deformity will be reduced if such women do not have any more children. Murphy (1940) presents data which show that in women who have given birth to one foetal monster the chance of bearing further defective children is 24 times greater than it is in the general population, which incidence he gives as 47 per 10,000 live births. (2) Because the frequency of malformed children increases after 30 years of age and much more after 40 years, couples should have all their children when the mother is less than 35 years and preferably less than 30 years. (3) A third way of slightly diminishing the number of abnormal babies is to consider performing abortions on women who contract German measles during the first three months of pregnancy.

We cannot keep previable infants alive, but, in some instances of placenta praevia and toxaemia, we can maintain pregnancy long enough to have the foetus remain in the uterus up to or beyond the time of viability. We do not know how to eliminate placenta praevia, and we cannot prevent abruptio placentae except in some cases by the proper treatment of toxaemia and the

prevention of trauma. We are also at a loss as to what to do about the small group of babies for which no cause of death can be determined clinically or at autopsy. Aside from these exceptions we possess measures of prevention and treatment which can salvage more than half the human beings whose lives are snuffed out thus early in their existence.

In my opinion a saving of foetal lives can be accomplished by (I) proper antepartum care, (II) prevention and treatment of prematurity, (III) prevention of birth injuries, (IV) prevention and early treatment of infections in the baby and of syphilis in the mother and in the baby, (V) prevention and early treatment of the toxaemias of pregnancy and (VI) avoidance and prompt treatment of foetal erythroblastosis.

I. *Proper Antepartum Care.* In obstetrics, as in other branches of medicine, prevention is not only of greater importance but also simpler than cure, hence physicians must familiarize themselves with the essentials of antepartum care. The latter means proper supervision of a pregnant woman so that she will be able to pass through pregnancy and labour without detriment to herself, and so that her new-born baby will be healthy after labour. The ideal situation is for every woman to have a thorough examination before she plans to become pregnant. If this procedure were carried out routinely, some abnormal conditions would be detected which are not found until pregnancy has begun and which, in some instances, lead to death of the mother or the child, or both. The laity must be made to realize that it is important for a pregnant woman to see a physician as soon as she knows that she is pregnant. This is not the place to discuss antepartum care but it is apparent that informed physicians who conscientiously supervise their patients during pregnancy accomplish the

following: determine if anaemia is present and suggest remedies to overcome it; make certain that the patient's diet is satisfactory; detect syphilis and institute intensive therapy as soon as the disease is discovered; prevent toxaemia and treat it intensively if it appears; detect clinically, or with the aid of roentgenography, a contracted pelvis or pelvic tumor which may necessitate an elective Caesarean section instead of ending up with a brutal, operative vaginal delivery; detect pulmonary tuberculosis, heart disease or other ailment which will require the use of a local anaesthetic instead of the more dangerous inhalation anaesthetics; discover serious illnesses, such as chronic nephritis, which sometimes make interruption of pregnancy imperative; detect diabetes and treat it in order to prevent the high foetal mortality that accompanies this disease; discover foci of infection and remove them; determine the Rh factor of the patient and, if negative, of the husband, in order to prevent and treat foetal erythroblastosis and so on.

Of great importance among the poorer classes of the population is an improvement in the standard of health and nutrition of the mothers, because infant mortality is greatly influenced by social and economic factors, as shown by Baird (1945) in Aberdeen.

II. *Prevention and Treatment of Prematurity.* The following resolution was accepted by the American Academy of Pediatrics (DeLee and Greenhill, 1947a) in 1935: "A premature infant is one who weighs 2,500 g. (5.5 pounds) or less at at birth (not on admission) regardless of the period of gestation. All live-born premature infants should be included, evidence of life being heart-beating or breathing."

The chief causes of prematurity are: multiple births, disturbances in the ovum (monstrosities), toxaemia, chronic nephritis, syphilis, placenta praevia, abruptio

placentae, serious maternal illnesses (pulmonary tuberculosis, heart disease and pneumonia), polyhydramnios, surgical operations on the mother, and habitual abortion.

The only causes of prematurity which are preventable or can be treated with a view to prolonging the intrauterine existence of a foetus are toxaemia, syphilis, some serious medical illnesses in the mother, mild cases of placenta praevia, and some instances of habitual abortion. Surgical operations, other than for acute diseases, should be postponed whenever possible, preferably until after labour. The immediate reason for the death of most otherwise normal premature infants is inability to obtain oxygen through inadequately developed lungs (Potter, 1944).

Not many hospitals have adequate equipment or sufficient personnel to care properly for premature infants. This is unfortunate because the lives of many of them could be saved by efficient care during the first day or days of life. Usually the physician must care for the baby during the first hours of its precarious life, whether delivery takes place in a hospital or at home and, after this, he must instruct someone else in this task. He must therefore possess the knowledge necessary to keep these infants alive whose management is far different from that of full-time babies.

He must remember that in premature babies there is a grave danger of cerebral haemorrhage and that analgesics and anaesthetics affect them adversely. Therefore unusual skill must be exercised in delivering them and the less analgesia and anaesthesia given the mothers the better it is for these infants.

Whenever a premature baby is expected in a hospital or at home, preparation must be made for its immediate care before labour ensues. It is best to deliver such babies in a hospital because during the first few days of life they require constant and skilful care every hour of the day and night. During the first stage of labour the mother should receive one or more doses of vitamin K as a prophylactic measure against bleeding in the premature baby.

Immediately after delivery a premature baby must be wrapped in a warm sterile blanket or towel. Its head should be lowered to permit the escape of mucus and secretion from the respiratory tract. It is best to wait until the cord stops pulsating before ligating it and while waiting for this to occur, the baby will obtain 30 to 60 ml. (1 to 2 ounces) of blood from the placenta.

Nearly all premature babies should be given oxygen through a catheter placed in the nose or mouth; the amount given should be about 120 bubbles per minute. Since cyanosis in these infants is frequent during the first few days of life, they must be watched closely all the time; otherwise occasionally a baby will be found dead in its bed. Premature babies must be handled as little as possible, visitors should be kept away from them and all individuals who come in contact with them must wear face masks to minimize the danger of infection to which premature babies are highly susceptible.

Premature babies require a fluid intake of one-eighth to one-sixth of their body weight in 24 hours and a food intake of 70 calories per kg. (2.2 pounds) after the first few days of life. Raw breast milk is the best food for them. A breast-pump may be used to obtain the milk from the mother or a wet nurse.

III. *Prevention of Birth-Injuries.* By birth-injuries I mean every type of harm that may befall a child during the process of birth. This includes asphyxia, haemorrhage into the brain and elsewhere, paralyses, fractures, distortions and injuries to the viscera. Whereas a few of

these injuries occur in spontaneous un-assisted labour, the vast majority result from lack of skill, poor judgment, haste, injudicious use of analgesia and anaesthesia and deliberate carelessness of and disregard for human life. At the time of birth we have abundant opportunity to reduce drastically the foetal and neonatal mortality. The performance of Caesarean section in the presence of such conditions as central placenta praevia and midplane and outlet contractions will save some babies who might otherwise die.

Cerebral haemorrhage accounts for many foetal deaths and for almost one-half of the fatalities among premature babies. In a large proportion of dead premature babies cerebral haemorrhage and asphyxia are present. Therefore all these factors (prematurity, cerebral haemorrhage and asphyxia) must be considered together.

"Asphyxia" is the term used universally to denote absence of breathing but it literally means "without pulse." The causes of asphyxia during labour are (1) conditions responsible for the direct cutting off of the supply of oxygen (suffocation) and (2) those in which the neurorespiratory system is depressed (paralytic). Asphyxia may be treated before birth as well as, or after delivery but prevention is far more important.

The prevention of asphyxia of the foetus *in utero* comprises the recognition and avoidance of its causes. Therefore the physician should direct labour into normal channels and intervene only when really necessary. The injudicious use of analgesics (specifically, morphine and the barbiturates), oxytocics (particularly pituitary extract and quinine) and general anaesthetics (especially the prolonged use of concentrated mixtures of nitrous oxide) will surely be harmful, especially to premature babies. Hurried or prolonged deliveries, an unduly long second stage,

badly performed forceps operations, hurried breech extractions and versions and extractions exact a high toll of foetal lives. Even Caesarean section does not assure the delivery of a live baby or one that will live, because if this operation is done after a long test of labour the baby may have been injured before the section was undertaken. Still more important, the baby is less likely to survive if abdominal delivery is resorted to in the presence of prematurity, if the mother has received large doses of analgesics and, particularly, if an inhalation anaesthetic is used for the operation. Therefore direct local infiltration or caudal anaesthesia is indicated when a Caesarean section is performed and the infant is premature. Likewise narcotics should be withheld until the baby is delivered.

A profuse maternal haemorrhage, with the loss of a large number of erythrocytes, may reduce the amount of oxygen the foetus should have. This may result in asphyxia of the foetus and is sufficient reason for the quick replacement of the blood lost in cases of placenta praevia, abruptio placentae and other conditions. In some instances it may be necessary to transfuse the baby immediately after birth and also to administer oxygen. The asphyxia which may result from haemorrhage is one argument against phlebotomy in eclampsia. The asphyxia that follows the excessive use of analgesics and anaesthetics is not only due to their direct effect on the respiratory centre of the body but also to the fact that these drugs depress the mother's respiration, both in frequency and in depth, and thereby diminish the supply of oxygen to the placenta.

The foetal heart-sounds should be auscultated at intervals of 30 minutes, or more often, in the first stage of labour and at least every 5 minutes in the second stage or even every 30 seconds if the delivery is difficult. At the first sign of foetal distress,

such as irregularity of the heart, watchfulness should be redoubled, the foetal heart listened to almost continuously and preparations made for operative delivery. In every case in which labour is prolonged or delivery from below is most likely to be difficult, vitamin K should be given to the mother at least 4 hours before delivery.

As soon as danger to the foetus is established, the treatment indicated is either removal of the cause of the anoxaemia or delivery of the child so that it can obtain air.

Waters and Harris (1931) were the first to emphasize that anoxia of the foetus can be recognized by a change in the foetal heart-rate and can be treated successfully by the administration of oxygen which prevents respiratory depression from anoxia. The response to such therapy is usually observed within 10 minutes and often is apparent in less than 5 minutes. If improvement does not occur within 15 minutes, it may be assumed that the administration of oxygen will be of no value. Usually more than 10 minutes is required to prepare a patient for operative delivery; this preparation can be carried out while the oxygen is being given. Frequently the improvement in the foetal heart-rate will obviate the necessity of exigent operative delivery and its dangers to the mother and the child.

A definite relation has been shown to exist between foetal oxygen-want and irreparable damage to the nervous system, which later in life manifests itself in neurological defects. The best outcome in cases of asphyxia is offered by rapid delivery but this may not always be possible and, further, the trauma incident to the operation may prove fatal to the infant. Hence great care must be exercised in the selection of the type of operation to be performed and the manner of its performance.

The treatment of asphyxia after delivery comprises four principles as follows:

(1) *Proper Position.* If a baby is delivered by means of a difficult forceps operation, version and extraction, or other forcible means there is a great possibility of the presence of cerebral haemorrhage or a susceptibility to such cerebral damage. Therefore in such cases a baby should not be placed with its head lower than its body. It should certainly not be held up by its feet because of the danger of initiating or aggravating a cerebral haemorrhage. On the other hand, if a baby has not been subjected to birth-trauma but has a large amount of fluid and mucus in the respiratory tract, its head should be lower than its body to aid drainage. . . .

(2) *Warmth.* All babies should be kept warm immediately after birth. It generally does not matter if a few minutes elapse between the birth of a normal full-time baby and attempts to keep it warm. On the other hand, in the case of premature and traumatized babies a few minutes of exposure to cold air or even to room temperature may mean the difference between life and death. Therefore, in every case, when a premature baby is about to be delivered and in all cases when the obstetrician is having difficulty in delivering a baby, preparations should be made by an assistant to receive the baby in warm blankets, towels, sheets or other coverings . . .

(3) *Clearing the Respiratory Passages.* The air-passages must be cleared after the baby is placed in a proper position and warmth is applied. It is dangerous to perform artificial respiration when the trachea, bronchi and sometimes the alveoli are full of amniotic fluid, meconium, blood or vaginal secretions, because the foreign substances would be forced still farther down and give rise to atelectasis, pneumonia and sepsis. . . . When the child is fully delivered, it is held up by the ankles, while the head rests on some flat surface, and in this position the throat is cleared. . . .

However, this position may be dangerous if cerebral haemorrhage exists.

If the baby does not gasp or if its attempt to do so reveals that the trachea is blocked, as indicated by retraction of the ribs and epigastrium, the air passages must be cleared. This is best done by means of a tracheal catheter.

(4) *Supplying Air or Oxygen to the Lungs.* One of the simplest ways to perform artificial respiration is to blow air gently into the baby's lungs through a tracheal catheter, but this should not be done until all mucus and other foreign material have been removed from the pharynx, trachea and bronchi (DeLee and Greenhill, 1947b).

Cerebral haemorrhage may occur without apparent cause, but usually it results from a fracture or rupture of a cerebral or meningeal blood vessel; this is sometimes caused by extreme overlapping of the cranial bones. It may also be due to asphyxia. The prevention of cerebral haemorrhage consists of the proper conduct of spontaneous and operative deliveries, the avoidance of oxytocic drugs before delivering the baby, the temperate use of analgesics, the proper handling of the newborn baby immediately after birth and so on. The value of vitamin K both as a prophylactic and as a therapeutic measure has been overrated. I agree with Potter (1945) that "no decrease in infant or foetal mortality can be expected from the routine administration of vitamin K to all women during labour." However, since there is no specific therapy for cerebral haemorrhage at the present time and since vitamin K does raise the prothrombin value of the blood of the newborn within 4 hours of its administration, it should be given immediately after delivery to all infants suspected of having cerebral haemorrhage and this should be done whether or not the mother received any of the vitamin during labour. Likewise all premature babies should receive vitamin K immediately after birth.

One way to prevent cerebral haemorrhage in some full-time babies, but especially in premature ones, is to perform a timely episiotomy. The removal of the barrier which exists at the perineum by an episiotomy will in my opinion definitely reduce the incidence of cerebral haemorrhage in premature babies. This is particularly true if local infiltration anaesthesia is used instead of inhalation anaesthesia because the latter definitely adds to the dangers of premature delivery. Likewise an episiotomy should be performed before all breech deliveries. The application of forceps to the after-coming head will save some babies.

Paralyses, fractures, distortions and injuries to the viscera and other parts can usually be avoided by the proper conduct of labour.

To-day Professors F. J. Browne and Ebbe Brandstrup are going to discuss the subject of induction of labour as a means of reducing foetal mortality. In 1936 Davidson, of the Rotunda Hospital, reported that he induced premature labour in 286 women during a period of 10 years. He lost 1 mother and 20 babies (7 per cent). Among these 286 induction cases, Davidson had to perform 9 Caesarean sections, 6 pubiotomies, 3 versions and extractions and 30 forceps deliveries. Lorincz (1940) carried out Davidson's recommendations. In an editorial comment on Lorincz's paper I (Greenhill, 1943) made the following statement to which I still subscribe to-day: "I am unalterably opposed to the induction of labour after the 36th or 37th week in cases of contracted pelvis in the hope of avoiding a Caesarean section. First vaginal delivery will take place without trouble at term in at least 75 per cent of all cases of contracted pelvis

regardless of the degree of contraction. In many of the remaining cases, delivery can be accomplished from below with some difficulty but, nevertheless, with no maternal mortality and with slight foetal mortality. Last, in the indisputable cases of cephalopelvic disproportion, a Caesarean section may be performed at term, preferably after a short test of labour. This can be accomplished with little danger to the mother or child.

" Induction of labour a few weeks before term carries a slight maternal mortality, chiefly from infection, and morbidity due to infection and haemorrhage because of a torpid uterus. There is also a high foetal death-rate due to prematurity and the trauma of prolonged and operative delivery." Two important items are difficult to determine with certainty: (1) that in a given case it is impossible for the baby to be delivered vaginally at term and (2) that if labour is induced prematurely the baby is sufficiently developed to survive. Since we cannot be sure of these points, it is far safer for the mother and the baby to wait until term and use the proper procedure at that time."

IV. *Acute infections in the newborn* can be reduced by strict asepsis and antisepsis during and after labour, the judicious use of analgesia and anaesthesia, proper handling of the baby following delivery and early diagnosis and particularly prompt treatment of infections with penicillin and the sulphonamides. Likewise a considerable reduction in the foetal death-rate can be accomplished in some parts of the world through treatment of women who have syphilis as early in pregnancy as possible and continued through the gestation. Of course, all babies born of syphilitic mothers must be examined carefully and treated promptly. At present the most effective and the least dangerous drug for syphilis is penicillin.

V. *The prevention of eclampsia* by adequate prenatal care is one of the greatest advances in the field of obstetrics. There is ample proof that eclampsia can be eradicated almost entirely by giving pregnant women proper antepartum care. Also a decided curtailment of the evil effects of pre-eclapmsia can be accomplished by the watchful guidance of parturient women. Unfortunately a large proportion of pregnant women throughout the world receive no antepartum care or only superficial consideration.

VI. The number of babies lost because of *erythroblastosis* is not large but it can be reduced by the routine determination of the Rh factor in all pregnant women, by performing periodic tests for antibodies during the second half of gestation in all women who are Rh negative and whose husbands are Rh positive, by making clinical and blood examinations at least twice a day of every second and subsequent baby born of a women whose blood is Rh negative and by giving blood transfusions to babies with erythroblastosis, using Rh negative blood, as soon and as often as it is indicated. The twice-daily blood examinations should be done for the first 3 days following birth.

The newer tests for the Rh-Hr types, as well as the development of methods of detecting the presence or absence of sensitization, now permit more accurate forecasting of the disease. It is important to recognize the differences in the three distinct clinical types grouped under the term erythroblastosis because diagnosis and treatment vary with the manifestations. Those cases characterized by anaemia and slight jaundice (congenital haemolytic disease) are readily cured by transfusions with Rh negative blood but the infants with severe jaundice and little or no anaemia (icterus gravis) usually die within a short time (Potter and Adair, 1943;

D'Esopo and Marchetti, 1942). According to Wiener and Wexler (1946) exchange transfusion with blood completely compatible with the maternal serum should apparently prevent the onset of the final process or arrest it after it has begun.

Yerushalmy (1945) has brought out additional facts about neonatal mortality. Factors which were found to be more closely associated with neonatal mortality relate to physical ones in the parents and in the infant. For example, the mortality of male infants is 25 per cent higher than that of female infants. Studies of a large number of births show that babies born to very young or very old mothers are exposed to a higher risk of early mortality than are those born to mothers in their twenties. Likewise the age of the father is also found to affect the mortality of his offspring. The lowest rates are found for second and third births and extremely high rates abound for infants of high parities. These factors were found to be as strikingly correlated with the incidence of premature birth as with neonatal mortality.

From a detailed analysis of neonatal mortality by the age of the mother and by parity, it can be shown that there appears to be an optimal interval between successive births. The neonatal mortality rate, as well as the incidence of premature birth, increases when the interval is either too short or too long.

There appears to be a familial tendency to stillbirths and neonatal deaths. Infants born to mothers who lost a previous child are exposed to a risk of early mortality more than twice that of those born to mothers whose entire previous issue survived. Premature birth was also found to be a repetitive character.

These associations suggest that genetic factors may be at least partly responsible for neonatal mortality and for premature birth.

CONCLUSIONS.

Foetal and neonatal death-rates are high all over the world. In spite of distinct improvement, it is still possible to reduce drastically the number of deaths. Careful autopsy studies have shown that the chief causes of death are prematurity, asphyxia, birth-trauma, malformations, pneumonia and maternal toxaemia. These 6 specific conditions are responsible for more than 70 per cent of foetal and infant deaths. At the present time many of these deaths are not preventable, particularly those due to monstrous development and to non-viability. However, a large number of babies can be salvaged by (1) proper ante-partum care, (2) prevention and treatment of prematurity, (3) prevention of birth-injuries, (4) prevention and treatment of infections, particularly pneumonia and syphilis, (5) prevention and early treatment of the toxaemias of pregnancy and (6) avoidance and prompt treatment of foetal erythroblastosis.

All specialists in obstetrics are aware of the causes and methods of preventing foetal and neonatal deaths, but unfortunately only a very small proportion of babies are delivered by obstetricians. The vast majority of pregnant women, all over the world, are cared for by general practitioners. It is the responsibility of those of us who are teachers of midwifery to give diligent training to our medical students and also to general practitioners. In the case of the latter this training can be attained by postgraduate courses in the proper conduct of pregnancy, labour and the puerperium. Only in this way can we hope to reduce not only the excessively high maternal mortality but also the frightful preventable number of foetal and neonatal deaths.

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Leucorrhoea in Pregnancy

(A further study with special reference to the hydrogen ion concentration and lactic acid content of the vagina)

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I. Introduction.

In this Journal Liston and Cruickshank (1940a) described certain methods by which they attempted to study the condition of 200 pregnant women who were believed to be suffering from leucorrhoea. They indicated that they considered that a further study was desirable in order to elucidate the fundamental causes of this common but often neglected complaint, and the present paper is the sequel.

The examinations were conducted in the Leucorrhoea Clinic of the antenatal department of the Simpson Memorial Maternity Pavilion of the Royal Infirmary in Edinburgh. This clinic was under the care of one of us (F. B. C.) during the period covered by the study, 1940–41. Another of us (W. G. L.) co-operated with her in the examination of the patients, while the

others (W. O. K. and A. P. T. E.) and Mr. Jacomb assisted in the elucidation of the chemical and physical problems which were encountered during the study.

II. General Nature of the Problem.

It is well known that the reaction of the vagina during the period from puberty to the menopause is definitely acid, the normal pH being in the range 3.8–4.4. Various workers have shown that lactic acid is present and Cruickshank (1934) has suggested that this lactic acid is very probably produced from glycogen, present in the vaginal epithelium, by Doderlein's bacillus which is normally the preponderating organism in the adult human vagina. It has also been demonstrated that, when the vagina is infected with certain other other organisms, the pH is usually high: for example in cases of vaginal thrush the average value is 4.8 (Liston and Cruickshank, 1940b), while in trichomonas

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The exigencies of the war prevented publication at an earlier date.

infestations it is 5.34 (Liston, 1940). The normal high acidity of the vagina evidently aids greatly in preventing the multiplication of the harmful organisms.

Though the importance of lactic acid in the vagina has been widely recognized, few attempts seem to have been made to determine quantitatively the concentration present. Certain figures were obtained at a comparatively early date by direct titration with alkali, but this gave only the total acid present and there was no guarantee that all or even a substantial proportion was lactic acid.

The scarcity of quantitative data concerning lactic acid in the vaginal secretion is no doubt mainly due to the difficulty of obtaining amounts of the secretion from individual cases adequate for accurate determinations.

It seemed possible that this difficulty of obtaining fluid might be largely overcome if use could be made of the washings obtained by the introduction of several cubic centimetres of a saline solution into the vagina. This is conveniently done by the pipette already described (Liston and Cruickshank, 1940a; Liston, 1940). The resulting wash-out · fluid consists of a mixture of the vaginal secretion and saline solution in a ratio depending on the abundance of the secretion. In order that the results obtained by the analysis of this wash-out may give information on the biochemistry of the original secretion it is necessary to know the proportion in which the 2 fluids have been mixed. This can be done by having some characteristic substance or indicator present in the saline solution in known concentration. The determination of this indicator in the mixture of secretion and saline solution gives the ratio in which those are present.

The object of the present investigation has been to obtain data concerning the pH and the lactic acid content of the vagina from a number of patients. In this way it was hoped to obtain information as to how far the pH is determined by the concentration of lactic acid present. Cytological and clinical observations were also made so that variations in lactic acid and the pH could be correlated with these findings.

III. SOURCE OF THE MATERIAL EXAMINED.

The material examined was derived from patients attending the Leucorrhoea Clinic of the Antenatal Department of the Simpson Memorial Pavilion. Pregnant women suffering from a discharge were sent to this clinic from the antenatal clinic of the Maternity Pavilion, and also pregnant women, who had been treated at the Venereal Diseases Department of the Royal Infirmary, were sent to be kept under observation at the clinic till they were confined. Other institutions also, chiefly concerned with the welfare of unmarried expectant mothers, sent women for examination to determine whether they suffered from infectious disease. A few pregnant women came to the clinic with letters from their doctors because they complained of discharge or irritation. These women were often not examined before their visit to the clinic, so it came about that among the pregnant women attending the clinic there were some who were not suffering from leucorrhoea and were found to be normal or approximately normal. A few women who had been attending the clinic before confinement appeared again for a further examination after delivery.

Among the 203 patients examined, many of them on a number of occasions, 192 were pregnant at the time of examination, while 11 were postnatal cases examined at various intervals (2 weeks to 10 months) after confinement.

B

IV. METHODS USED FOR THE EXAMINATIONS.

(a) *In the Clinic.*

(b) *In the Laboratory.*

(a) *Methods used in the clinic.* These methods have been described in detail in a number of papers (Liston and Cruickshank, 1940a, 1940b) and it is necessary here only to give an outline of the procedure. The patient is first interrogated in the doctor's private room. The kind of questions which should be put to her have been detailed in the papers referred to above. The patient is then conducted to the examination room, where she is placed in the proper position on the operating table by a nurse.

Under good illumination an inspection of the vulva and adjoining parts is made, including the orifice of the urethra. Smears on slides are made when necessary. Thereafter a bivalve speculum is introduced into the vagina. The cervix is clearly defined. The glass vaginal pipette, charged with 5 ml. of the diluting fluid, is introduced into the posterior fornix. By appropriate manipulation of the pipette and rubber bulb the vagina is washed with the diluting fluid and this fluid is thereafter aspirated back into the glass bulb of the pipette. The pipette is now withdrawn from the vagina. A small drop of the washed-out fluid in the tip of the pipette is placed on each of 2 glass slides. A loopful of stain, methylene blue or neutral red, to which a little glycerine or serum has been added to prevent rapid evaporation, is mixed with one of the drops on the slide. In the same way a loopful of Lugol's Iodine solution, to which a little glycerine has been added, is mixed with the diluted discharge on the other slide. The material on both slides is covered with cover-glasses and then examined under a microscope to note: (a) the proportion of epithelial cells to pus cells; (b) the type of bacterial flora present —I, II, or III; (c) the presence of such parasites as *Trichomonas vaginalis* or the blastospores or pseudomycelium of the fungus *Oïdium albicans* which is the cause of thrush; and (d) in the preparation to which the iodine had been added, the amount of glycogen stored in the epithelial squames. The method of gauging the amount of glycogen in the epithelial cells of the vagina is illustrated by reproductions of coloured micro-photographs in Plate II of the paper on "Leucorrhoea of Pregnancy" published in this Journal (Liston and Cruickshank, 1940a).

This examination of the patient and of the wet films permits of a rapid diagnosis being made and the selection of a suitable line of treatment. Further, the patient is instructed to bring with her at her next visit to the clinic a sample of her urine collected an hour or so after the main meal of the day, to be tested for the presence of albumin and sugar. The need to collect the sample at a special time is explained in a paper on "The Glycosuria of Pregnancy" (Liston and Chisholm, 1941).

Meanwhile the patient's vagina has been cleaned and dried with swabs, while the pipette is replaced in its stand properly marked with the patient's identification number. In a similar way, slides made for subsequent staining and study in the laboratory are numbered. When the clinic is finished, the slides and pipettes are transferred to the laboratory, where they are subjected to a further examination as follows:

(b) *Method of procedure in the laboratory.*

(1) *The determination of the* pH *of the diluted discharge from the vagina.* This should be determined as soon as possible after collection. In the present series this was done on a Beckman pH meter. This determination of course gives the pH of the

diluted secretion and not of the original vaginal fluid, but as the latter is appreciably buffered, while the diluting fluid is not, the change in the pH is not likely to be significant. This matter has been discussed and tested by Oberst and Plass (1936) who showed that the vaginal secretion in most cases can be diluted with distilled water to 15 ml., but not to a greater extent, without notable changes in the pH. The quantity of diluent used in the examination of the present series, 5 ml., is well within the safe range to avoid any material alteration in the pH of the vaginal contents by the dilution.

Liston and Cruickshank (1940a; 1940b) have shown that the pH readings obtained by the use of the Beckman pH meter do not differ from those obtained by the capillator method of the British Drug Houses Ltd., provided always that the instructions for this method of estimating the pH are closely followed. The capillator or colorometric method can be used if a suitable pH-meter is not available.

(2) *The measurement of the degree of dilution of the discharge.* It has been explained that in order to obtain information regarding the biochemistry of a discharge which has been diluted it is necessary to know the proportion in which the fluids have been mixed and this can be done by the use of an indicator in the diluting fluid.

A suitable indicator for measuring the degree of dilution must satisfy several conditions. It must be stable, non-toxic and non-irritant, and it must be capable of being quickly and accurately determined when present in small concentration. Further, the indicator must not interfere with the determination of the lactic acid, or alternatively it must be easily removed so as to eliminate such interference.

After various trials the best indicator was found to be potassium thiocyanate, which could be introduced into the saline solution (0.85 per cent NaCl) in a concentration of $N/50$. When a solution of a ferric salt is added to the wash-out fluid so prepared, a deep-red colour of ferric thiocyanate ion is developed and photometric readings can be made on a Zeiss stufophotometer. A simple calculation then gives the proportion of vaginal secretion present.

The use of potassium thiocyanate as an indicator has two drawbacks which, however, can be overcome:

(1) If protein is present in the washings in appreciable amount, a precipitate or opacity is formed on the addition of the ferric salt and the estimated degree of dilution is too high. It is therefore desirable to precipitate the proteins with trichloracetic acid before adding the ferric reagent.

The importance of this interference by proteins was not realized during the earlier part of this work. Later on precipitation with trichloracetic acid was introduced and applied to all fluids though only occasionally could the original method have led to serious error.

(2) Thiocyanate seriously interferes with the determination of lactic acid by the method employed, namely that of Quastel and Gordon (1939), according to which the lactic acid is oxidized by ceric sulphate to aldehyde and the latter absorbed in bisulphite and titrated with iodine as in the older method of Friedmann, Cotonio and Shaffer (1927). Cerdic sulphate acts on thiocyanate with the formation of sulphur dioxide and, presumably, it is in consequence of the reaction of the latter with acetaldehyde, as it is formed, which results in the method giving results much below the proper values.

It is therefore necessary to remove all the thiocyanate from the fluid before carrying out the lactic acid determination. This is conveniently done by precipitation with silver acetate. Sufficient of this reagent must be added to precipitate the chloride

as well, otherwise the precipitation of the thiocyanate may not be complete.

Determination of the percentage of discharge in the vaginal washings.

Solutions required: (1) Trichloracetic acid 20 per cent in water. (2) Ferric indicator solution. Iron alum, 5 g., is dissolved in water, 50 ml., heat being applied if necessary. Concentrated nitric acid, 50 ml., is added and the mixture boiled to expel nitrous fumes. After cooling, water, 150 ml., is added. (3) Stock thiocyanate solution used for the vaginal washings. This contains potassium thiocyanate $N/50$ and sodium chloride 0.85 per cent.

Procedure. To 3 ml. of the 20 per cent trichloracetic acid is added 0.2 ml. of the vaginal washings. This should be measured with an absolutely dry 0.2 ml. pipette. The discharge is thoroughly washed out of the pipette by alternately sucking in and expelling its contents in the trichloracetic acid solution. The mixture is filtered or centrifuged and 1 ml. of the clear fluid is added to 1 ml. of distilled water followed by 2 ml. ferric indicator solution. The light absorption or extinction coefficient of a 5 mm. layer is then measured on the stufophotometer, the blue filter S47 being used. We shall call this reading R^1. It is necessary next to take 2 further readings, first a blank on equal quantities of the ferric indicator and water and we shall call this reading A^1. A second reading on a mixture of equal quantities of the ferric indicator and a solution prepared exactly as in the first part of the first test solution R^1, save that the 0.2 ml. of the washed out discharge is replaced by 0.2 ml. of the stock thiocyanate solution. We shall call this reading B^1.

Calculation of the percentage of the discharge in the washings.

It is not difficult to show that the percentage of discharge present in the washings is given by the formula

$$100 \left[1 - \left\{ \frac{\log A^1 - \log R^1}{\log A^1 - \log B^1} \right\} \right]$$

An example may make this clear. The reading on the stufophotometer of solution R^1 was found to be 29.2, that of A^1 87, and of B^1 23. When $R^1 = 29.2$, $A^1 = 87$ and $B^1 = 23$.

Then

$$100 \left[1 - \frac{1.9395 - 1.4654}{1.9395 - 1.3617} \right]$$

$$= 100 \left[1 - \frac{.4741}{.5778} \right]$$

$$= 100(1 - .8206)$$

$$= 100 \times .1794$$

$$= 17.94 \text{ per cent of discharge in the mixture.}$$

In order to test the accuracy of the method a series of dilutions of serum in 0.85 per cent saline was prepared and 0.2 ml. of each dilution was treated exactly as above. The results obtained are shown in the following table.

Actual dilution, per cent	Found dilution, per cent
10	9.8
15	14.7
20	19.9
25	24.9
30	29.2

(3) *The precipitation of thiocyanate preparatory to estimating lactic acid.*

Having ascertained the percentage of the vaginal discharge in the washings from the vagina, it is now necessary to estimate the quantity of lactic acid in the mixture. In order to do this the first step in the procedure is to remove the thiocyanate because it interferes in the estimation of the lactic acid by the method adopted.

The solutions required for this purpose are a solution of silver acetate, 0.25N in

0.02N sulphuric acid. To 2 ml. of the diluted vaginal discharge is added 14 ml. of the silver acetate solution. The precipitated silver salts are filtered off and a measured sample of the filtrate, preferably the whole of it, is used for the lactic acid determination.

(4) *Lactic acid determination.*

The method of Quastel and Gordon (1939) was closely followed and we need not repeat the details. It may, however, be mentioned that it was found unnecessary to employ a current of nitrogen to carry over the acetaldehyde from the oxidation mixture in the Schroeder apparatus to the absorption tube, as air may be safely used instead. It appeared that the important point was that the current of air should be sufficiently strong. A water pump attached to the Schroeder apparatus so as to draw a current of air through in the proper direction was found very satisfactory. The air was not specially washed before entering the oxidation chamber but the determinations were carried out in a room free from fumes. When the determinations were made on solutions of zinc lactate of known strengths, the results varied from 98 to 100 per cent of the theoretical.

If the sample of filtrate used for the lactic acid determination after treatment with the silver acetate amounted to X ml. (2 ml. had been added to 14 ml., that is, 2 in 16, or 1 in 8), and it was found to contain Y mille mols. of lactic acid, then in the washed out discharge there were $8Y/X$ mille mols. per ml., and if the washed out mixture contained Z per cent of the original secretion, the latter contained $\dfrac{8Y \times 100}{XZ}$ mille mols. per ml. or mols. per litre.

It is to be noted that the substance estimated by the above method may consist of lactic acid or a salt such as sodium lactate or more usually in these experiments a mixture of both. We shall therefore frequently refer in the following pages to the total lactic concentration and we shall call this T.L. There is an obvious convenience in calculating this as mols. per litre (M) instead of milligrams per cent, as by so doing it is unnecessary to make any assumption as to whether the lactic acid molecule is present as acid or salt.

V. GENERAL SURVEY OF THE RESULTS.

On account of limited space it is not possible to give the separate results of all examinations but a brief survey on a statistical basis may be useful. This will include the results of all the examinations we made except those where the proportion of discharge in the washings was less than 8 per cent. When the washings contain relatively little discharge the possibility of error in our results, especially in the estimate of T.L., becomes relatively greater, being inversely proportional to the amount of discharge in the mixture. For this reason the results of the examination of some 40 samples have been excluded from our tables.

We have set out our results in 2 tables, I and II. Table I shows that 254 samples were examined for both lactic acid concentration, T.L., and for pH. The samples have been divided into 10 groups. Each group, except the last, covers a range of T.L. concentration of 0.005 mols. of lactic acid per litre; the last group includes all samples with more than 0.045 mols. per litre T.L. The highest observed concentration was 0.104 M. In the second column of the table is stated the number of samples falling within each group, and in the third column the mean of the observed pH values of these samples. In the fourth column is given an estimate of the standard deviation of the frequency distribution of the individual pH values in each group; this figure provides an indication of the degree of

scatter of the pH values of the fluids, all of which had approximately the same T.L. In the fifth column is given the standard error of the mean pH for each group. This standard error of the mean is, of course, dependent on the standard deviation of the distribution of the individual observations (as given in the previous column) and also on the total number of observations from which each mean is calculated. In the final column we give values of the mean pH for each group calculated from the equation $\overline{pH} = 5.861 - 47.0 \times$ T.L. (equation A), the mean T.L. for each group (0.0025, 0.0075, 0.0125 . . .) being used in the calculation.

linear relationship over this range of T.L. is confirmed. Indeed the actual mean pH for the first group (T.L. less than 0.005) also differs from the calculated $\overline{pH}$ by less than twice the standard error, but here the standard error is relatively large in consequence of there being only 11 observations, and so the agreement is less significant. The last groups (T.L. greater than 0.040) obviously depart from the linear regression line, but both of them contain a very small number of samples.

The results presented in Table I show, as might be expected, that the amount of lactic acid present in a fluid has an important effect in determining the pH value. The

<div align="center">TABLE I.</div>

<div align="center">Compares T.L. with pH.</div>

Groups of T.L. concentrations in mols. per litre	Number of samples in each group	Mean pH of each group	Standard deviation of individual values	Standard error of the mean pH	pH calculated from equation A
0.000–0.005	11	6.03	0.664	0.200	5.74
0.005–0.010	25	5.63	0.477	0.095	5.51
0.010–0.015	35	5.25	0 344	0.058	5.27
0.015–0.020	42	5.01	0.527	0.081	5.04
0.020–0.025	40	4.69	0.397	0.063	4.80
0.025–0.030	36	4.60	0.382	0.064	4.57
0.030–0.035	34	4.39	0.262	0.045	4.33
0 035–0.040	17	4.12	0.190	0.046	4.10
0.040–0.045	7	4.45	0 661	0.250	3.86
Over 0.045	7	4.19	0.242	0.091	—
Total	254				

Some explanation of the method of obtaining this equation is required. Preliminary inspection suggested that, apart from the first and the last two groups in the table, the mean pH varied approximately uniformly with the T.L. A linear regression line was therefore fitted to the 229 individual observations in the 7 groups of T.L. from 0.005 to 0.040. In this way was obtained equation A. As will be seen, the difference between the actual mean for each group and $\overline{pH}$ as calculated is less than twice the standard error of the mean in each of the 7 groups, so that the existence of a

linear relationship between mean pH and T.L. over a wide range is rather unexpected, and it suggests that, on the average, the fluid must be fairly uniformly buffered in the pH range from about pH 4.0 to pH 5.6. The individual fluids, of course, do not follow the equation A, and this implies that factors other than the T.L. concentration play a part in determining pH. For example, the fluids may be buffered to different extents. However, it is clear that any reduction in the rate of formation of lactic acid in the vagina will tend to increase the pH, and so, when

glycogen is deficient in the epithelial cells, it is not surprising that the pH tends to be raised, for, as we have remarked above, it is generally agreed that the lactic acid is derived from glycogen. In the discussion in the next section we shall notice several examples of high pH associated with low glycogen content.

Table II classifies our results according to the clinical diagnosis of the cases. It shows that 203 patients were examined; of these, 192 were pregnant at the time of our

ments. In all, 440 samples were examined for pH and 263 samples for lactic acid concentration, T.L. Each determination of T.L., of course, required more time than the rapid estimation of pH with the glass electrode and Beckman pH meter; this circumstance accounts for the larger number of samples in the pH than in the T.L. series. Some of the patients were examined only once, but many were examined several times and were studied over a period of months; during this period they,

TABLE II.

Results Classified according to the Clinical Diagnosis of the Cases.

	Clinical diagnosis	Number of cases	Number of samples	Mean pH	Number of cases in which T.L. was determined	Mean T.L. of group in mols. per litre	pH calculated from equation A
Pregnant cases	Normal cases	32	43	4.38	29	0.032	4.36
	Small erosions	18	27	4.42	18	0.030	4.45
	Medium erosions	10	17	4.64	6	0.022	4.83
	Large erosions	14	38	5.32	21	0.018	5.02
	Uncomplicated thrush	27	61	4.63	39	0.026	4.64
	Thrush and erosion	9	19	4.72	7	0.019	4.97
	Thrush and trichomonas	14	47	4.93	23	0.025	4.69
	Uncomplicated trichomonas	63	161	5.11	106	0.020	4.92
	Trichomonas and erosion	5	12	5.58	7	0.015	5.16
	Postnatal cases	11	15	6.17	7	0.006	5.58
	Total	203	440		263		

Pregnant women examined   192
Postnatal patients   11
All types of erosion   56
All trichomonas cases   82
All thrush cases   50

examination, while 11 had been comparatively recently delivered; they were examined at periods varying from 2 weeks to 10 months after confinement. Among the pregnant women there were 32 cases adjudged to be normal. The remaining pregnant women were all suffering from leucorrhoea attributed to cervical erosions, vaginal thrush, or an infestation of *T. vaginalis* or a combination of one or other of these conditions. The 11 postnatal cases had all suffered from leucorrhoea due to one cause or another before their confine-

were under treatment. It has not, in general, been found possible to give an account of individual cases in this paper, and all the available results, including, where possible, several from the same patient, have been used in compiling Tables I and II.

It is of some interest, for each type of case, to calculate the average pH which, on the basis of equation A, should correspond to the mean T.L. for that particular group as given in column 6 of Table II. These calculated values are shown in

column 7. It will be seen that this calculated value is, in general, in fairly good agreement with the average value of the observed pH in each group shown in column 4. This suggests that the effect of the lactic acid in determining the reaction of the fluid is not substantially modified by the disease conditions studied. A slight qualification to this conclusion may be required by the fact that in 4 of the categories, namely large erosions, thrush *plus* trichomonas, trichomonas *plus* erosions, and uncomplicated trichomonas, the observed average is slightly higher than that given by the equation A. It happens that those conditions are all of such a nature that in them we might expect serous fluid derived from the ulcer or from inflammatory tissue to contaminate the vaginal fluid proper, and this extra amount of buffering material would partly neutralize the lactic acid and so result in a somewhat higher pH than would otherwise be found. The small deviations must not be unduly stressed, but the results seem to be consistent with this interpretation.

Table II, like Table I, gives only average findings for each type of case; the individual results naturally show considerable variation. It brings out the tendency of each type of case to be associated with a certain degree of acidity, whether this is measured in pH or T.L. The connexion between acidity and clinical type might have been still more clear-cut if the observations had not included a number made on patients in the course of treatment. Such treatment of, for example, a trichomonas infection, often resulted in the disappearance of the parasites, a rise of glycogen in the cells of the vaginal epithelium, and an increase of the acidity. Such a case, though still recorded as one of trichomonas infection, gave results approximating to those characteristic of the normal individual, and, for this reason, the trichomonas group, on

the average, is not so far removed from the normal group as it would be if only untreated cases were included.

It is now necessary to discuss each group of cases somewhat more fully.

DISCUSSION OF THE VARIOUS TYPES OF CASES.

The result of the study of this series of 200 cases of leucorrhoea in pregnant women very closely conforms to the findings obtained in the first series of similiar cases which has already been published in this Journal (Liston and Cruickshank, 1940a).

The normal standard of the vaginal contents of healthy pregnant women.

We have shown in these studies that the vaginal contents of a normal pregnant woman present the following characteristics:

(1) Desquamated epithelial cells are more numerous than pus cells. (2) The epithelial cells are loaded with glycogen. (3) The bacterial flora consists of an almost pure culture of Doderlein's bacillus, i.e. Type I flora. (4) The acidity of the vaginal contents measured as pH varies between 3.8 and 4.4. (5) The concentration of lactic acid in the discharge has a mean value of 0.032 M. (mols. per litre).

Erosions.

Closely resembling the normal condition are certain cases which show a small erosion of the cervix. Those cases, so far as the contents of the vagina are concerned, can be distinguished from the normal by the presence of a larger number of pus cells, slightly less glycogen in the epithelial cells, a bacterial flora with a few rather smaller, gram-positive bacilli than Doderlein's organism, i.e. a bacterial flora of Type II, a less acid state of the vagina indicated by a rise in the pH to 4.42 and a decrease in the concentration of lactic acid to 0.030 M.

epithelial squames

trichomonas vaginalis

pus cells

PLATE I.

Smear from discharge of pregnant woman suffering from trichomonas vaginalis infestation. Stained by Best's carmine method and haemotoxylin, to demonstrate the presence of glycogen in some of the epithelial squames and in the bodies of trichomonas vaginalis which have been distorted in making the film. ×250

G.L.

glycogen laden desquamated epithelial cells

vaginal epithelium; the superficial layer shows squames filled with glycogen

PLATE II.

Section of the vagina of a female infant five days after birth, stained by Best's carmine method and haemotoxylin, to demonstrate the presence of glycogen in the superficial layers of the epithelium of the vagina. Some of the glycogen-laden squames have been desquamated into the lumen of the vagina. ×250

As the size and extent of the erosion of the cervix increases the abnormal features of the vaginal contents noted above become more and more accentuated until in cases with very large erosions pus cells become much more numerous than the epithelial cells in the discharge, and at the same time the discharge becomes more abundant. Such desquamated epithelial cells as are present in the discharge are found to contain less glycogen. Red-blood cells may also be present. The bacterial flora becomes even more mixed, gram-negative organisms of various kinds now preponderate and the bacterial flora passes gradually through II to Type III. The pH rises in medium erosions to 4.64 and in large erosions to 5.32. The lactic acid concentration falls considerably — to 0.022 M. in medium erosions, to 0.018 M. in large erosions.

We are satisfied that all erosions are not due to the same cause; some, particularly the smaller varieties, may have a physiological origin, but the larger erosions have undoubtedly a pathological basis. Lacerations of the cervix during previous confinements and septic infection thereafter, one theory of the origin of erosions, can play a small part in their causation, for as many as 35 per cent of the women we examined who showed erosions were primiparae. The cause or causes of erosions is still obscure and the condition calls for further study. Perhaps the most helpful line of approach to this investigation will be found in physical and chemical characteristics of the cervical secretion. Erosions frequently complicate other forms of leucorrhoea.

Vaginal thrush.

Patients suffering from vaginal thrush constitute about 25 per cent of the cases of leucorrhoea in pregnant women. The condition is easily recognized by finding the pseudo-mycelium or the blastospores of the fungus. The leucorrhoea of thrush may be uncomplicated or it may be associated either with an erosion of the cervix or with the presence of *T. vaginalis* in the vagina. In 27 uncomplicated cases the pH was found to be 4.63; this figure is the mean of 61 examinations (Table II). The lactic acid concentration in uncomplicated thrush estimated in 39 samples gave a mean concentration of 0.026 M. When thrush is associated with an erosion of the cervix, or with the presence of *T. vaginalis* in the vagina, the pH rises, in the former case a mean pH of 4.72 was obtained as the result of the examination of 19 samples and in the latter case a mean pH of 4.93 based on 47 examinations. The concentration of lactic acid also decreases to a mean of 0.019 M. when thrush is associated with a cervical erosion and to a mean of 0.025 when associated with *Trichomonas vaginalis*; those figures are based on 7 and 23 examinations respectively.

The material we obtained from the series of examinations now under consideration enabled us to make a special study of this condition and our findings have been published in 2 papers (Liston and Cruickshank, 1940b; Liston and Chisholm, 1941) which should be consulted. A brief resumé of these papers may be of use here.

There has been much confusion in the nomenclature of this disease and in the naming of the parasite which causes it. Our reasons for calling the disease Vaginal Thrush and the parasite which causes it, *Oïdium albicans* (Robin), are discussed at length in the first of the two papers mentioned above. We suggest the abandonment of such terms as " *Monilia* " and its derivatives, associated in the recent past with this disease, and we especially depreciate the use of the word " yeasts " to describe the blastospores, the resting and resistant forms of this fungus. The fungus, once it has secured a footing in the body in some moist acid situation such as the

vagina or the mouth, may invade other parts of the body such as the skin or nails, or the intestines and air passages. In the latter situations in infants it may cause serious symptoms, sometimes ending in death from diarrhoea or bronchitis. The cause of these deaths is frequently not recognized. Debilitated persons, and particularly young infants, are liable to suffer from this malady.

The parasite exhibits a predilection for glucose and this substance appears to be necessary to help the parasite to establish itself in the body. It is for this reason that the parasite is peculiarly liable to attack persons suffering from diabetes mellitus or, a matter of importance in our present discussion, pregnant women suffering from the glycosuria of pregnancy. This subject has been fully discussed in the second paper referred to above. It may be of interest to note that babies, who are sometimes fed with glucose as a cheap substitute for lactose, readily become infected with the parasite.

While gentian violet is an excellent antiseptic with which to combat the parasite, the conditions favourable for the growth of the parasite must not be overlooked. The parasite flourishes best in the vagina when the reaction is in the neighbourhood of pH 4.8; that is to say when the vaginal contents have a slightly less acid reaction than normal. It is remarkable how the parasite, and the symptoms caused by its presence, spontaneously disappear on the completion of labour. This change is associated with a marked decline in the acidity of the vagina at this time, a subject which will be discussed later.

It should be noted that the blastospores, the resting and resistant forms of this parasite, are widely scattered in the neighbourhood of infected persons, so that the danger of introducing infected women into a maternity hospital when young infants are present is evident. This fact, therefore, demands the early detection and treatment of vaginal thrush in the antenatal department. The detection and prevention of vaginal thrush at the clinic is facilitated by keeping a lookout for women suffering from glycosuria. How this can be done is discussed in the second paper referred to above.

Vaginal Trichomoniasis.

The commonest cause of leucorrhoea in pregnant women is the infestation of the vagina by the parasite *Trichomonas vaginalis*. Among the 200 women at present under consideration, *T. vaginalis* was found in the vagina in approximately 40 per cent. *Trichomonas vaginalis* may be found alone or it may be associated with erosions of the cervix or with the fungus which causes thrush. In uncomplicated *Trichomonas* infestation the vaginal contents have a pH reaction of 5.11. This is the mean figure of 161 examinations in 63 patients. The lactic acid concentration in 106 examinations gave a mean figure of 0.020 M. When the thrush parasite complicated the presence of *T. vaginalis* the contents of the vagina were slightly more acid, yielding a mean pH reaction of 4.93 in 47 examinations; the lactic acid concentration being then 0.025 M. the mean of 23 examinations.

When Trichomonas infestation was combined with a cervical erosion, a less common complication than with a thrush infection, these cases showed a less acid reaction, a pH of 5.58, the mean of 12 examinations. In the same circumstances the concentration of lactic acid was also lower, 0.015 M. being found as the mean of 7 examinations.

The material collected in the series of examinations under discussion afforded an opportunity to make a special study of this parasite and other similar parasites found in man and other animals. This study has

been published separately (Liston, 1940) and should be consulted. Here we can only mention some of the salient points concerning the leucorrhoea caused by the presence of ·this parasite, *Trichomonas vaginalis*, in the vagina of pregnant women.

It should be noted that while there are at least 3 species of *Trichomonas* parasitic on human beings, each species appears more or less to confine its attention to particular sites in the body. *T. tenax*, for example, inhabits the mouth, *T. arden-delteili* the large bowel and *T. vaginalis* the vagina. The latter, with which we are at present concerned, seldom invades other organs than those immediately adjacent to the vagina ·such as the urethra and the bladder.

This parasite, so far as we have been able to determine, does not produce resting or encysted forms and so we believe that infection takes place by more or less intimate contact with infected persons. Two sisters, for example, occupying the same bed, may infect one another. Males, too, may become infected from females, a husband from his wife, for example, and *vice versa*. In males the parasite lives either beneath the prepuce, in the urethra, in the bladder, or in the ureter. Such cases have been reported by Liston and Lees (1940) and others.

Another species, found in cattle, *T. foetus*, is known to be spread by infected bulls. This species causes abortion in cattle and is therefore of economic importance. *T. foetus* may, indeed, invade the uterus from the vagina, its normal habitat, and there cause pyometra.

So far as we know, *T. vaginalis* does not cause abortion nor does it often invade the uterus, but generally confines its attention to the vagina where, in acute cases, it may cause severe inflammation, producing symptoms which are often mistaken for gonorrhoea. But in pregnant women the disease is most often met with in a subacute or chronic form, often symptomless except for the presence of leucorrhoea.

Apparently *T. vaginalis* lives upon glycogen (Plate I) and flourishes in a slightly acid medium, the most favourable pH being around 5.3. Such conditions are found in the vagina of certain women in whom the amount of glycogen in the epithelial cells is less abundantly present in that situation than normal, and in consequence these cases show a rather higher pH reaction than normal.

This parasite is readily killed by various drugs, such as acetarsol, for example, to mention only one of numerous preparations used. It is, however, very difficult to eradicate this organism completely from the vagina, especially in chronic cases. The parasite possibly finds shelter from the local action of these drugs beneath the epithelium in the subepithelial tissues. We have not been able to demonstrate the presence of the parasite in this situation, possibly because of the limited facilities for obtaining suitable material for sections and also because of the difficulty in fixing so delicate an organism *in situ* in the tissues. The rough, or granular feeling of the mucous membrane of the vagina so characteristic of the chronic forms of this disease and the presence of haemorrhages below the ·epithelium, as well as the resistant nature of the infection support the view that the parasite can find shelter in this way from the local action of drugs inserted in the vagina. We have found, too, in sections, fragmented nuclear material below the epithelium, but it was not arranged in such a way that we could say it was derived from definite parasites. Wenyon, however, has shown in sections that the trichomonas *T. arden delteili*, which inhabits the lower bowel of man, may penetrate the epithelium and be found in the submucous tissue.

Trichomonas vaginalis often disappears from the vagina after labour and may not be

found there for some time, but, in the end, after some weeks, or months, it appears again in the vagina when the conditions become favourable for its multiplication.

Girls, before puberty, are not subject to infestation with *T. vaginalis*. It is generally believed that until puberty the reaction of the vagina is not acid nor is glycogen then present in the epithelial cells. It is the absence of glycogen, the food on which this parasite lives, which is probably the most important factor in preventing the growth and multiplication of this parasite in the young female.

We have made sections (Plate II) which show that at birth glycogen is abundantly present in the epithelium of the vagina but during the course of the first and second week of life this glycogen-charged epithelium is desquamated and is discharged from the vagina. It has been argued from this fact that the presence of glycogen in the epithelium of the vagina in the newborn infant is the result of the action of a hormone derived from the mother which is transferred to the infant before birth through the placenta and that it is the absence of this hormone in the infant after birth which causes a halt to the deposition of glycogen in the epithelial cells. At the age of puberty, however, when the young female can produce the hormone herself, the deposition of glycogen in the epithelial cells of the vagina is restored and then conditions become suitable for the parasite *Trichomonas vaginalis*.

A further study of this glycogen deposition process in the epithelial cells of the vagina seems to be called for. As a first step to this end, data regarding the vaginal contents of all normal females, young and old, should be collected.

Postnatal Cases.

Unfortunately the number of these cases examined is small and the findings are complicated by the fact that all of these women had suffered from leucorrhoea before they were confined. Still, two characteristic features pertaining to them all are well brought out in Table II, viz., the mean pH, calculated on 15 samples, is as high as 6.17 and this is associated with a remarkably low T.L., 0.006 M. estimated as the mean of 7 samples. Here we have another example of a fall in T.L. and a rise in pH associated with the disappearance of glycogen from the epithelial cells of the vagina. How has this sudden shedding of the glycogen laden epithelium at parturition been brought about? Has the action of the hormone which is supposed to cause the deposition of glycogen in the vaginal epithelium been checked or counteracted by the endocrine secretion of a gland such as the pituitary, called into activity in the course of labour, or has the action of the hormone which caused the deposition of glycogen in the vaginal epithelium been deflected to some other purpose as, for example, the production of milk in the breasts? Quite recently our attention has been drawn to the fact that coincidently with the shedding of the glycogen laden epithelium of the vagina of the newborn infant the mammary glands are frequently stimulated to such an extent that those glands enlarge and colostrum, even milk, may be secreted for a time. Actually stimulation of the breasts may be observed in infants of both sexes.

We need not speculate further but urge the collection, on the lines detailed above, of more facts relating particularly to the vaginal contents of healthy women after their confinement. Our findings are based on small figures obtained on women who had suffered from leucorrhoea and to that extent are unreliable.

It is an interesting and rather striking fact that practically always women infected with *T. vaginalis* or *O. albicans* fail to show the presence of these parasites in the vagina

shortly after parturition and the clinical symptoms due to the presence of these parasites disappear. We consider that this clinical improvement is probably due to the change in the pH of the vagina, which in these cases has risen to such an extent that conditions are no longer suitable for the growth of these two parasites.

In conformity with this view we have observed that when the glycogen reappears in the epithelial cells and the T.L. concentration rises so that the pH falls, the patients which formerly harboured *T. vaginalis* again become infested with the parasite. On the other hand, *O. albicans* often disappears permanently after parturition.

It seems probable that these changes, consequent on parturition, are the result of the rapid decrease of glycogen in the epithelial cells at this time. As long as the glycogen remains deficient, lactic acid is not formed and the acidity of the vagina remains low. We have seen that a similar change occurs in the female infant shortly after birth.

CONCLUSIONS.

1. A large number of specimens of vaginal fluid from pregnant women, mostly suffering from leucorrhoea, have been examined in respect of pH and lactic acid concentration. A method has been devised for dealing with the small quantities of vaginal fluid available by using a wash-out fluid containing $N/50$ sodium thiocyanate; the thiocyanate acts as an indicator of the degree of dilution of the vaginal fluid. The lactic acid as determined includes both the free lactic acid and lactate and is denoted by the letters T.L. (total lactate).

2. The acid state of the vaginal fluid in pregnant women is closely related to the amount of T.L. present in it. A linear regression equation has been calculated which gives the average pH of fluids which contain a given concentration of T.L. The average pH values found experimentally agree well with those predicted by this equation for values of T.L. less than 0.040 M.

3. Various instances have been referred to where the rise in pH with the associated fall in T.L. is accompanied by a disappearance of glycogen from the epithelial cells of the vagina. These observations are consistent with the view that the lactic acid is derived from glycogen.

4. The vagina in the normal healthy pregnant woman has a reaction in the neighbourhood of 4.38, the mean T.L. being 0.032 M. These conditions are associated with the bacterial flora of Type I and very few pus cells are present, but the epithelial cells of the vaginal wall contain abundant glycogen.

5. A reduction of the normal acid level with a decrease in the amount of glycogen in the epithelial cells and a fall in the T.L. give rise to conditions favourable for the development of certain parasites.

6. When the acid reaction of the vagina falls to a point around a pH of 4.8 the parasite of thrush, *Oïdium albicans*, can flourish provided it has been able to secure a foothold; this is facilitated by the presence of glycosuria.

7. When the acidity of the vaginal contents falls to a point at which the pH is about 5.3 the conditions are favourable for the growth of *Trichomonas vaginalis*. In such cases of Trichomonas infection very little glycogen is found in the epithelial cells and the concentration of T.L. is relatively low (average value 0.020 M.).

8. Shortly after parturition the pH of the vaginal contents rises to a point around 6. Glycogen is practically absent from the epithelial cells and the T.L. is very low (average values 0.006 M.). Conditions then are no longer suitable for the growth and development of *T. vaginalis* or *O.*

albicans; the symptoms due to these parasites consequently disappear. When, however, the acid state of the vagina returns, cases which previously showed *T. vaginalis* often relapse and the organisms reappear in numbers in the vagina. On the other hand, *O. albicans* often disappears permanently after parturition, especially when glycosuria comes to an end.

We are indebted to Mr. R. S. Barclay for assisting with the statistical calculations in Tables I and II, and to Mr. Kenneth Nicholson for technical assistance in the early stages of this work.

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Causes and Treatment of Tubal Occlusion[*]

BY

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Incidence of the Condition.

Failure to conceive is commonly due to a summation of minor factors—Meaker's infertility factors. Many reported analyses of large series of cases of sterility are surprisingly evasive as to the actual incidence of individual factors, but it appears to be commonly accepted that occlusion of the Fallopian tubes, relative or absolute, is the commonest single cause of sterility. Estimates of the incidence of all degrees of tubal occlusion vary between 18 per cent and 50 per cent of all cases of sterility. Siegler (1945a) describes tubal occlusion as the sole or a contributory cause in 50.6 per cent of his patients. Macomber (1929) found 13.4 per cent of " closed tubes " in his series of cases. Green-Armytage (1936) found that 34 per cent of his patients with primary sterility had impairment, complete or partial, of tubal function; and Rubin (1945a) estimates the corresponding incidence in his patients at 47 per cent.

It is important to differentiate between the incidence of tubal occlusion in sterile marriages as a whole and in cases where the female partner is at fault, and it is not always clear whether different authors are considering the percentage-incidence among female defects or among combined defects. It is, of course, impossible to ascertain accurately the number of cases where

" catarrhal occlusion " has prevented pregnancy, since it is generally considered that the satisfactory results which may follow a single insufflation or lipiodol injection are due to removal of a mucous plug, even though such obstruction is not noted at the time.

The results of treatment of sterility in general can never be accurately assessed, as chance must play an important and often unknown part in producing a successful issue. We all have experienced cases where, without any treatment, pregnancy occurs after 3 or more years of infertility, and also cases where pregnancy follows 6 or 12 months after insufflation, and it is tempting to claim that pregnancy in the latter group has been directly due to the treatment given. When, however, definite tubal occlusion can be demonstrated, whether complete or partial, and when treatment is logically directed towards the cure of the obstruction and a pregnancy results when the obstruction has been demonstrably overcome, success may be claimed as absolute and is correspondingly more satisfying.

The findings about to be discussed are based on a survey of approximately 860 sterile marriages. In 60 patients complete occlusion of the Fallopian tubes, of varying origin, was found to be present and in many other women definite defects in the function of the tubes, without complete occlusion, were undoubtedly contributory causes of the infertile mating.

The Aetiology of Occlusion.

The condition may be primary or secondary, complete or partial; in the latter case the tube may be anatomically patent but functionally defective, so that the ovum cannot readily pass along it. Into this category comes the rigid and fixed tube following inflammatory infiltration of its wall, and the tube which is grossly elongated around a parovarian cyst or broad ligament fibroid (Fig. 1). Intact cilia and normal peristalsis are probably necessary for the transmission of the ovum, and it is possible that the normal tube may even be capable of applying its fimbrial end to the ovary during dehiscence, though this latter function cannot be an essential one, since many pregnancies have occurred with absence of one tube and of the opposite ovary, implying that the ovum must be able to traverse several centimetres of peritoneal space.

Even tuberculous tubes may be patent, but conception in that case must be extremely rare, even without endometrial tubercle and with normal ovulation. I do not know of a genuine case, although I believe some have been claimed.

The primary type of tubal occlusion is commonly associated with genital hypoplasia. It seems to be generally agreed that this condition is one of the most frequent causes of infertility, and Siegler (1945b) and others have pointed out that the undeveloped tube may be partly or completely occluded, elongated or convoluted, and that poor contractility is often present in such cases. Spasm is common in the hypoplastic type of tube, and it has been suggested by Kurzrok and Lieb (1930) that human semen can affect uterine and possibly tubal muscular contraction and relaxation, and that in some cases of sterility there is an abnormal degree of spasmodic contraction of the tube in response to seminal absorption.

Signs of Hypoplasia.

Genital hypoplasia is too often diagnosed on very slender grounds, and such a diagnosis is not acceptable if based merely on the finding at routine pelvic examination of an apparently small and acutely anteflexed uterus, or a "congenital retroflexion." The uterine index of Meaker is a useful guide but, even where there is definite disproportion between the length of cervix and body, indicating the undeveloped type of uterus, pregnancy may occur quite readily and go to term, suggesting that there has been no true functional hypoplasia of uterus or tubes. Many women in whom true hypoplasia of the genital tract is present have general evidence of deficient sexual development in the contours of the body, in a history of late menarche, scanty or irregular menses and frigidity or diminished libido; but there commonly occur cases in which the frame of the woman as a whole, her menstrual history and sexual response, give no hint of deficiency, yet there is a small uterus, with microscopic evidence of deficient development of the endometrium in all phases, and tubes which are patent only at high pressure, with spasm, if at all. There may also be stenosis of the tubes in such cases, indicated by the kymograph.

It is well recognized that in the absence of contraception and with complete and regular sexual intercourse, conception may not occur within 12 months or more of the first coitus, and Green-Armytage (1943) among others has pointed out that the average duration of normal sex-relations before conception is 6 months. It has been suggested that final development of the female genital tract may depend on the absorption of some substance present in seminal fluid but doubt has been cast on the validity of this. Whatever the mechanism involved, it seems likely on general grounds

that the delay in conception commonly encountered in the first few months of marriage may be due to incomplete genital development in which the Fallopian tubes share. Whether there is actual non-patency of the tubes in such cases has not usually been demonstrated, but among the eventual pregnancies in my series of cases of sterility are 3 in which there had been found adequate evidence of genital hypoplasia, including microscopic confirmation of endometrial deficiencies, with tubal occlusion to insufflation and to lipiodol. In these 3 cases no treatment was given, as the patients defaulted during the investigation, but subsequent follow-up indicated that pregnancy had ultimately occurred after a lapse of a year or more, presumably due to ultimate canalization of the previously occluded tubes.

Incidence of Hypoplasia.

The incidence of hypoplasia as a cause of occlusion is evaded in many statistical surveys, but the more reliable estimates suggest that hypoplasia in one form or another is the major cause of approximately one third of all cases of female infertility. I have found adequate reason to diagnose genital hypoplasia in approximately 28 per cent of all types of tubal occlusion. In many of these cases the occlusion was only relative, but in a significant number complete occlusion was found and overcome, though not necessarily with a successful issue in the shape of a pregnancy.

The secondary type of occlusion is, of course, usually associated with inflammation which may be tuberculous, puerperal or gonococcal. The Americans find gonococcal infection to be the chief cause of secondary tubal occlusion, but the incidence of the disease in this country certainly seems to be very much less than in the States and I have suspected its existence in relatively few of my own cases.

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Occlusion, partial or complete, may also be produced by tumours, especially cornual adenomyomata, but elongation or compression of one or both tubes may be produced by parauterine cysts or fibroids.

Peritoneal Haemorrhage Causing Occlusion.

Not an uncommon finding in cases of complete tubal occlusion is distortion of the tube with involvement of the fimbrial end in a mass of adhesions between ovary, broad ligament and lateral wall of the pelvis. In many of these cases there is no past history to suggest infection, nor is there microscopic evidence of such, but sometimes altered blood is found in and around the mass. Such cases may simulate endometriosis and in fact some are due to this curious pathological condition, but in others it would appear that there has been haemorrhage into and around a corpus luteum or follicular cyst, and biopsy does not confirm endometriosis. It must be admitted, however, that the microscopic diagnosis of endometriosis limited to the ovary is very difficult.

Secondary occlusion of the tubes especially at the fimbrial end, is of particular interest from the surgical point of view in that it may be overcome by insufflation and that major surgery may be justifiable and successful in a proportion of such cases, especially if there are no other abnormalities present in either husband or wife.

Apparent occlusion, absolute or relative, may occur as a result of premenstrual swelling of the endometrium in the region of the cornua, associated perhaps with spasm of the tubes; and Lane-Roberts et al. (1939) suggest that if the tubes are apparently occluded to insufflation in the premenstrual phase repetition a few days prior to ovulation is essential. It is my own practice now, wherever possible using

a kymograph, to carry out insufflation in the first place on the 8th or 9th day of the cycle even though this may necessitate another later examination to obtain an endometrial biopsy in the secretory phase.

DIAGNOSIS.

Dangers of Insufflation.

First and foremost amongst means of diagnosis must come Rubin's test. It is of value as a therapeutic measure as well as

the test is carried out, but most of us must have had the experience at some time or other of the patient, apparently perfectly healthy, who produces a most alarming fainting attack after trivial manipulation of the cervix. Sudden death from attempts at criminal abortion are probably usually due to fairly gross damage of the uterus, but a sufficient number of cases have been recorded where there was no doubt that the abortionist had proceeded no further than insertion of a sound or syringe inside the

FIG. 3.

Kymographic record of tubal occlusion due to spasm, resolving into patency but with defective peristalsis. In this case a diagnosis of genital hypoplasia was made on clinical, kymographic and histological grounds.

being a diagnostic necessity. It can be carried out without anaesthesia and with negligible risk, although cases of collapse and even of air embolism have been reported. Such cases must usually be due to an error of judgment regarding the amount of gas allowed to flow or the time at which

external os and yet the patient had collapsed and died within a few minutes.

Nevertheless, the procedure of insufflation is carried out very widely as an out-patient diagnostic method in innumerable clinics throughout this country and in America and, with proper care, no signi-

ficant ill-effects should occur. It has the indisputable advantage that not only may patency be proved by auscultation, but a kymographic record may be obtained showing the behaviour of the tube and thus evidence of spasm or defective peristalsis can be placed permanently on record, and subsequent tracings after treatment may be compared with the original (Fig. 3).

Insufflation with Biopsy.

Though insufflation may be carried out alone, it has an advantage over other methods of tubal investigation in that it may be combined if desired with endometrial biopsy in either the proliferative or the premenstrual phase. Information from biopsy is, of course, only applicable to the particular cycle during which biopsy is made, and if abnormalities are demonstrated, other than tuberculosis or similar active disease, a repetition of the biopsy in subsequent cycles is desirable. Biopsy can be carried out without anaesthesia, but if it is to be done, there is much to be said for carrying out the whole operation under anaesthesia, when full dilatation of the cervix may be achieved, a procedure which possibly has value as a somewhat empirical form of treatment.

Possibility of tuberculosis of endometrium.

Some authorities consider that biopsy should be avoided in the initial investigation and treatment of primary sterility, but in my view it has an important part to play in the diagnosis not only of endocrinal causes of infertility but also of the aetiology of tubal occlusion. Tuberculosis, often symptomless, is a significant cause of sterility, usually with tubal occlusion, but in some cases without demonstrable occlusion. The disease may be suspected by reason of a previous history of abdominal tuberculosis. It is important to exclude it as certainly as possible and, short of

laparotomy, endometrial biopsy is the only satisfactory means. Opinion varies as to the incidence of tuberculosis as a cause of sterility, and claims up to 15 per cent of all cases have been made. My own experience indicates that the incidence is of the order of 8 per cent of all cases fully investigated, although I have suspected it in others who did not permit full investigation.

Endometrium and Pelvic Inflammation.

Some pathologists, including especially Harvey (1944) of Edinburgh, hold the view that the endometrium may reflect, to some extent, remote pelvic inflammation by producing an infiltration of plasma cells and other evidence of chronic inflammatory reaction—a true chronic endometritis. Although at first sceptical of this suggestion, I have become convinced that there may be some truth in the theory as I have many times received a hint from the pathologist in his biopsy report of the probable presence of chronic pelvic inflammation, not otherwise suspected, and have subsequently had the opportunity at laparotomy of finding positive microscopic or naked-eye evidence that it existed.

A defect of insufflation is that little evidence is obtainable as to the state of the individual tubes. Whether or not an accurate distinction can be made, by auscultation, between patency of the right and of the left tube is doubtful, but this is perhaps a point of minor importance as, in any case where insufflation leads to a suspicion that there is deficient function of the tubes, X-ray examination can be done.

Comparison with Hysterogram.

Many attempts have been made to compare the results of insufflation with those of salpingogram. Sharman (1939) states that in 104 cases in which the dual investigation was carried out, there were only

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2 in which lipiodol demonstrated patency where the tube had appeared occluded to insufflation. I consider that the difference in the results of the two methods is much greater and have demonstrated patency to lipiodol in a considerable number of cases where repeat insufflation had indicated occlusion, but I still prefer to make the initial investigation by insufflation with carbon dioxide rather than by lipiodol, and I am supported in this view by Rubin's statement that lipiodol is statistically more productive of ill-effects than insufflation.

X-ray Investigation.

X-ray visualization of tubes, or hysterosalpingography, has a rather different function to perform in diagnosis, and is particularly applicable to cases apparently occluded to insufflation, or where there is a past history suggesting that tubal occlusion will be present. I prefer to use fluid neohydriol rather than the corresponding viscous preparation, and I have no personal experience of the use of any other form of opaque fluid except the original lipiodol, but many attempts have been made to find a more suitable medium for demonstration of the tubes and Titus and others (1937) have described the use of a mixture of mono-iodomethane sulphonate of sodium with acacia. Other substances have also been tried because of the view that there is risk of a flare-up of a chronic pelvic inflammation if lipiodol is used, but such an accident is not a common occurrence. In my own experience of insufflation and lipiodol-diagnosis in cases of sterility or pelvic pain, covering approximately 2,000 separate operations, I have records of only 4 cases showing any ill-effects, and in only 2 of these was significant pelvic inflammation produced. In one the husband was azoospermic and no permanent harm was done; in the other there may have been an extraneous source of infection after the operation and, in fact, a pregnancy did occur during the next menstrual cycle after the apparent pelvic inflammation, so again no real harm was done.

The chief advantage of the use of lipiodol is that the site of occlusion or stenosis can be demonstrated, the possibilities of surgical relief assessed and, furthermore, minor degrees of congenital or acquired malformation of the uterus may be disclosed which would otherwise be missed. It is most essential to carry out lipiodol-injection under the X-ray screen and preferably without anaesthesia, so that the behaviour of the tubes under injection can be seen. An X-ray picture taken after injection should be followed by a further plate 24 hours later (Fig. 4).

Spread of lipiodol over the peritoneal cavity from patent tubes within a few minutes after injection may sometimes obscure the outline of the tube and uterus and may even merge with any traces of leakage into the vaginal vault. Lipiodol which is encysted in peritoneal adhesions, or contained in a hydrosalpinx, is always readily differentiated in a 24-hour plate from that which is diffused freely throughout the peritoneum, and it is my experience than any vaginal spill disappears completely within 24 hours. In fact I have been satisfied recently with repetition after 4 or 5 hours in cases where a patient came from an outlying place and did not wish to stay overnight in hospital or to make another long journey next day (Figs. 5 and 6).

The type of cannula used for injection of gas or lipiodol deserves some attention and most well-known workers in the field of sterility have developed their own instruments. In my experience the type sometimes known as the Leech-Wilkinson cannula is one of the most effective. The fact that it screws into the cervix suggests that it might cause damage to tissues and pain to the patient but I have used it in a

large number of cases now, especially where occlusion is present and considerable pressure has to be employed, and I am satisfied that it gives the most accurate joint between cervix and syringe, that the patient suffers minimum discomfort compared with that caused by grasping the cervix with a volsellum and, finally, that the cervix suffers no significant or permanent damage. Little pressure is required where the tubes are patent, and in such cases a simple acorn pattern of cannula is all that is required, without any application of traction to the cervix.

TREATMENT.

Methods of treatment of tubal occlusion fall naturally into 3 groups: medical measures, chiefly hormonal, attempts at overcoming obstruction by insufflation or lipiodol and, in a small group of cases, major surgical procedures. The very means adopted in diagnosis are of course, often therapeutic in that there is a fairly high incidence of pregnancy following a single operation of insufflation or lipiodol-injection, even when no evident lesion is present. It has been suggested, therefore, that catarrhal occlusion may be present in an otherwise normal tube and may be overcome by the passage of gas or fluid.

It is, however, only too easy to attribute success to insufflation and Rubin's (1929) principles should always be the guide—success must not be attributed to insufflation unless pregnancy occurs within 2 menstrual cycles following insufflation in a case of sterility of at least 3 years' duration, without other evident cause for the sterility and where no other treatment is given parallel with the insufflation. We all have records of patients who undergo a so-called investigation consisting of "dilatation and curettage and insufflation" after 2 years of doubtful infertility and who become pregnant a year or so later. In such cases it is most unlikely that the operation has been responsible for the "cure".

Possible Effects of Time.

The effects of chance and the lapse of time play a part—often the only part—in the cure of many sterile marriages. It may be that in such cases there is gradual improvement of genital hypoplasia, or spontaneous correction of anovular cycles, or improvement in the general health of the husband and of his seminal fluid. A recent analysis of a series of first pregnancies in women over 30 has given reason for scepticism concerning some claims to success in the treatment of infertility. Out of 113 women having their first confinement at the age of 30 or more, 53 had no valid history of infertility, but 48 had been married with regular marital relations for at least 4 years without admitted contraception, and pregnancy had occurred for no very evident reason at the end of that time without any treatment.

In only 12 cases, out of a total of 60 women with 4 years or more of infertility, had any treatment been adopted to improve fertility. Any one of the remaining 48 cases might well have chosen to attend a sterility clinic after 4 years of fruitless marriage, have commenced an investigation with insufflation, and produced a pregnancy immediately afterwards when, no doubt, her case would have gone to swell the total of "cures".

Repeated Insufflation or Lipiodol-Injection.

Most writers on the subject of infertility suggest that insufflation or lipiodol-injection, in the absence of demonstrable pelvic pathology, is followed by pregnancy in a high proportion of cases. Rubin (1945b) claims success in 21.6 per cent of cases where the tubes have been apparently completely patent; 25.6 per cent in

" partial patency " (with repeated trials), and 6.16 per cent in cases of non-patency (presumably by repeated attempts until patency was achieved). Green-Armytage (1936) claimed 43 per cent of pregnancies following lipiodol injection, and other workers quote figures of the same order.

Siegler (1945c) states that the operation may require performance 10 or 12 times, and Kotz and Parker (1939) suggest an average of 6 tests for each successful pregnancy. Most people consider that it is possible to break down fimbrial occlusion by repeated passage of gas or oil, and it is even suggested that peritubal adhesions may be broken down, permitting freer movement in the tubes. Moore-White (1940) considers that preliminary treatment with oestradiol benzoate assists in promoting success with insufflation.

Spasmodic Occlusion.

In assessing the value of repetition, it must be remembered that spasm of the tubes may simulate complete or partial occlusion on several occasions, with apparent complete patency ultimately due to variation in the same patient in the response of the tubes on varying occasions. This must apply particularly to cases where preliminary insufflation is carried out without anaesthesia and final success achieved under general anaesthesia, possibly due to the abolition of a tubal irritability by the anaesthetic. In a number of my own cases initial occlusion to carbon dioxide, even under anaesthesia, has yielded to the rather slower flow of fluid neohydriol without anaesthesia, and I think that in at least a proportion of these cases the tubes have actually been patent all the time, but that spasm occurred on the first occasion due to the sudden impact of gaseous distension on the uterus. Lipiodol-injection should certainly be attempted if insufflation gives rise to any doubts.

Various measures may be adopted in an endeavour to overcome spasm; an injection of atropine intravenously has sometimes appeared to produce patency after about 30 seconds in tubes hitherto impervious to gas and, on several occasions, I have repeated the insufflation or lipiodol-injection a second time, giving an intramuscular injection of 20 mg. of oestradiol benzoate 24 hours before the test, and have proved patency on this second occasion.

Again must be emphasized the insidious effect of time, for a success after repeated insufflations may really be a success due to the lapse of a year.

Personal Experiences.

The foregoing words cast doubt on the validity of the claims of some enthusiasts. One does not doubt the accuracy of the figures quoted, but it does seem possible that insufficient credit has been given to nature. I now have records of about 130 pregnancies out of a total of over 800 cases of sterility the records of which have been collected. Not all these cases received full investigation, since under war-time conditions defaulting inevitably occurred; for the same reasons a postal follow-up of defaulters failed to trace a big percentage of those in whom records were incomplete. The proportion of pregnancies among fully treated cases is very much higher than among those who defaulted at an early stage, but analysis of successful pregnancies indicates that chance played the sole part, or was an important contributory factor, in 28 per cent of all cases. Among the failures (to date) occlusion of the tubes, complete or partial, was present in over 40 per cent (including those in which gross male defect was also present). Although 28 per cent of the " cures " followed soon after one or more insufflations or lipiodol tests, of all women in whom insufflation was

carried out only 30 per cent became pregnant, and the incidence of success in the series treated, solely as a result of insufflation or lipiodol injection, cannot be more than 10 per cent.

This is not intended as a counsel of defeat, and there is no doubt that the chances of pregnancy are improved by one or more therapeutic tests of the tubes. Even though other factors are present, including minor male defects, the procedure should be carried out.

Hormone Therapy.

Since Clauberg demonstrated, in 1938, that non-patency of the Fallopian tubes might be overcome by oestrogen therapy, much attention has been paid to this method of treatment, and it has been suggested that oestrogen compounds might even be of use where occlusion was due to the effects of disease. Moore-White (1940) has produced further evidence of improvement of function in abnormal tubes by the administration of oestradiol benzoate and suggests that, especially in occlusion at the fimbrial end, patency might be more readily established by insufflation at lower pressure after oestrin therapy.

Some cases of success may in fact be due to improvement in tubal spasm rather than to development of hypoplastic tubes or to recanalization of a secondarily occluded canal, but this possibility in no way invalidates a trial of hormone therapy when occlusion has been found, although it is probably useless and might even be harmful in tuberculous cases. A dosage of 5 to 10 mg. of oestradiol benzoate each week during the first 2 weeks of each cycle has been recommended: an alternative method is the use of one of the newer aqueous suspensions of crystalline oestrone, which permit of a slower and more continuous absorption of oestrogenic hormone, without risk of disturbances of menstrual rhythm or of suppression of pituitary activity. Subcutaneous implants of ovarian follicular hormone merit trial for similar reasons.

Effects of Artificial Oestrogens.

Whether or not the artificial oestrogens can produce a similar effect appears as yet undecided, and most workers seem to prefer natural oestrogens, but I have 6 cases of pregnancy in previously genuinely sterile women, following cyclical stilboestrol therapy given on the grounds of uterine hypoplasia as demonstrated by menstrual history, uterine proportions and other evidence. In only 2 of these cases had insufflation and lipiodol tests indicated partial tubal occlusion; in the others this procedure had not been carried out. Again, the factor of time cannot be excluded.

Effects on Cervix.

Recently attention has been drawn to the probability that oestrogens, possibly even artificial ones, alter cervical secretion and overcome "cervical hostility". It may be that a proportion of the apparent successes following oestrogen therapy are due to such a cervical effect rather than to any effects on the tubes, but at least there is ample evidence that oestrogens, properly used, have a beneficial effect in cases of infertility, especially of hypoplastic origin, and also that tubal patency can be produced by such therapy in cases of relative and even complete occlusion.

In 30 of my own "sterility cures" in which tubal occlusion was present, complete or partial, there is evidence that success could be attributed in large measure to hormone therapy in 11 cases, 8.5 per cent of all "cures". Patency has been achieved, apparently by hormones, in other cases of occlusion although pregnancy has not occurred to date.

Other Medical Measures.

Heat-therapy and even ultra-violet light have been used in an endeavour to overcome tubal occlusion, although in most cases it has been directed towards known pelvic inflammation. Its value in the treatment of inflammation is undoubted and it is thus a valuable measure for the prevention of permanent occlusion.

The value of irradiation of any kind in the actual treatment of long-standing tubal occlusion, with quiescent inflammatory changes, needs further investigation, but it is to be noted that Inglis (1943) states that he achieved patency by insufflation following the application of intra-vaginal heat in 7 cases out of 8 where tubal obstruction had previously failed to respond to insufflation alone.

Surgical Treatment.

In few aspects of gynaecology is such extreme difference of opinion expressed as on the value of surgery in the treatment of tubal occlusion. That obstruction due to fibroids or adenomyomata or other tumours may be overcome by abdominal operation is doubted by none, but where disease lies in the tube itself the outlook appears to be regarded as unsatisfactory, though numerous plastic operations have been devised.

In obstruction of the uterine end of the tube the distal part has been implanted into the uterus, with various modifications of technique to ensure patency, and even resection of intermediate occluded parts with end-to-end anastomosis has been attempted but most reports are not encouraging. With fimbrial occlusion the prospect of success seems greater and the possibility of ectopic pregnancy less.

Von Graff (1936) records 70 tubal implantations up to 1936, with 23 successful pregnancies. Bonney (1937) reports 18

per cent of successes of which 5 occurred after implantation and Green-Armytage's (1937) figures include 25 salpingostomies with 4 pregnancies and 3 implantations with 1 pregnancy.

Results of Various Authorities.

Siegler (1945d) considers operation justifiable and estimates the probability of successful pregnancy at 10 per cent after patency has been established: he found patency in 18 out of 23 cases with pregnancy in 4. Solomons (1935) reported a large series of 366 operations with 98 patencies, 30 becoming pregnant; and Cary (1941) collected 22 pregnancies out of 232 operations, but of these 4 ended in abortion and 7 in ectopic pregnancy. On the other side, Forsdike (1936) condemned surgery of the intermediate part of the tube on the strength of 10 unsuccessful operations, though he admits that operations on the fimbrial end offer rather better prospects.

The chief difficulty in operative repair of occlusion is that subsequent adhesions may cause further occlusion, and attempts to prevent this have included the use of saline and paraffin in the peritoneum, early lipiodol or insufflation to break down adhesions, and the use of various substances around the tubes to prevent the formation of adhesions.

Use of Allantoin.

In 1939 Gepfert published experimental work on the use of cow's allantoin, claiming that this substance prevented adhesions, and in 1943 the same author quoted 23 operations with 3 pregnancies as a result, in 2 patients.

Use of Amnion.

For the past 5 years, in the Department of Gynaecology at Newcastle General Hospital, salpingostomy has been carried out

FIG. I.
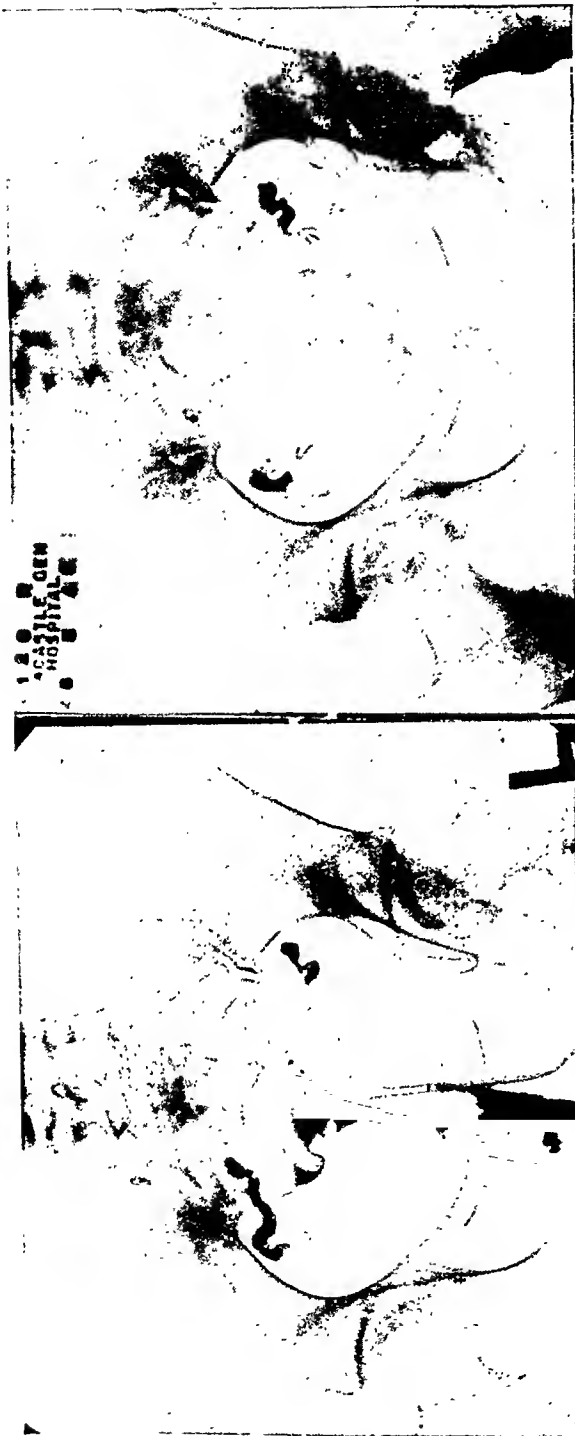
Lipiodol-hysterogram showing one example of partial tubal occlusion.

L.S.
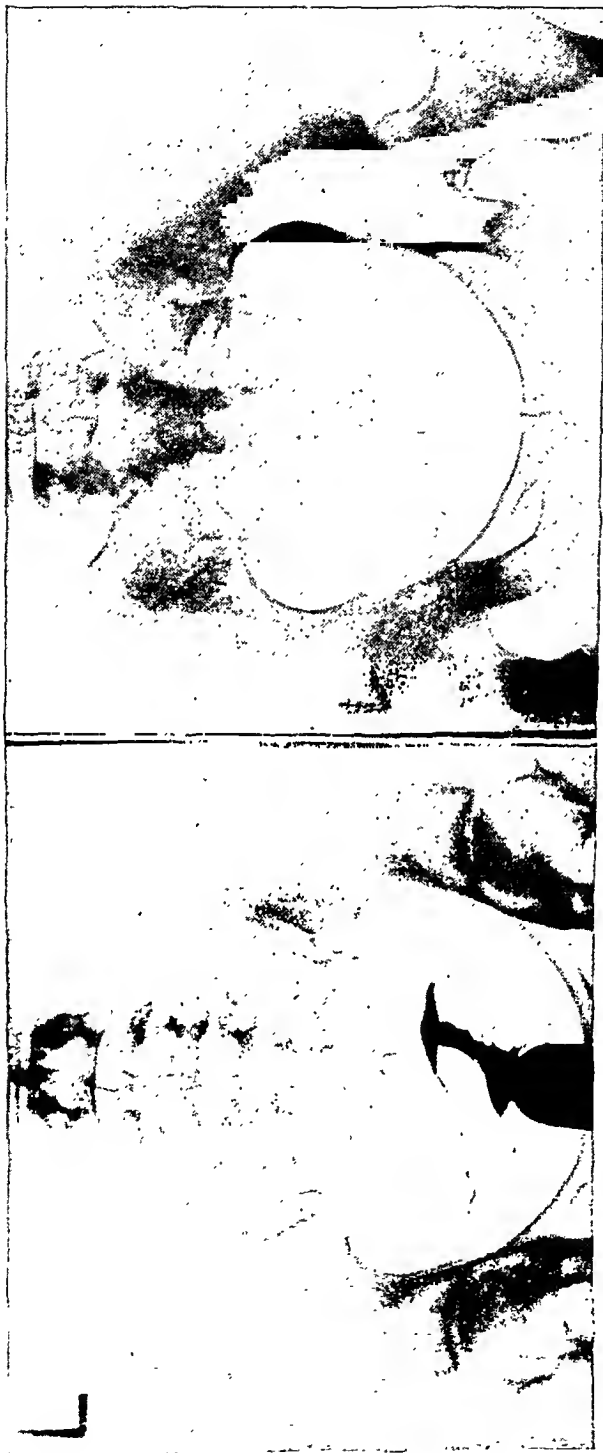
FIG. 2.

Lipiodol-hysterogram showing complete tubal occlusion, probably due to uterine and tubal hypoplasia.

L.S.
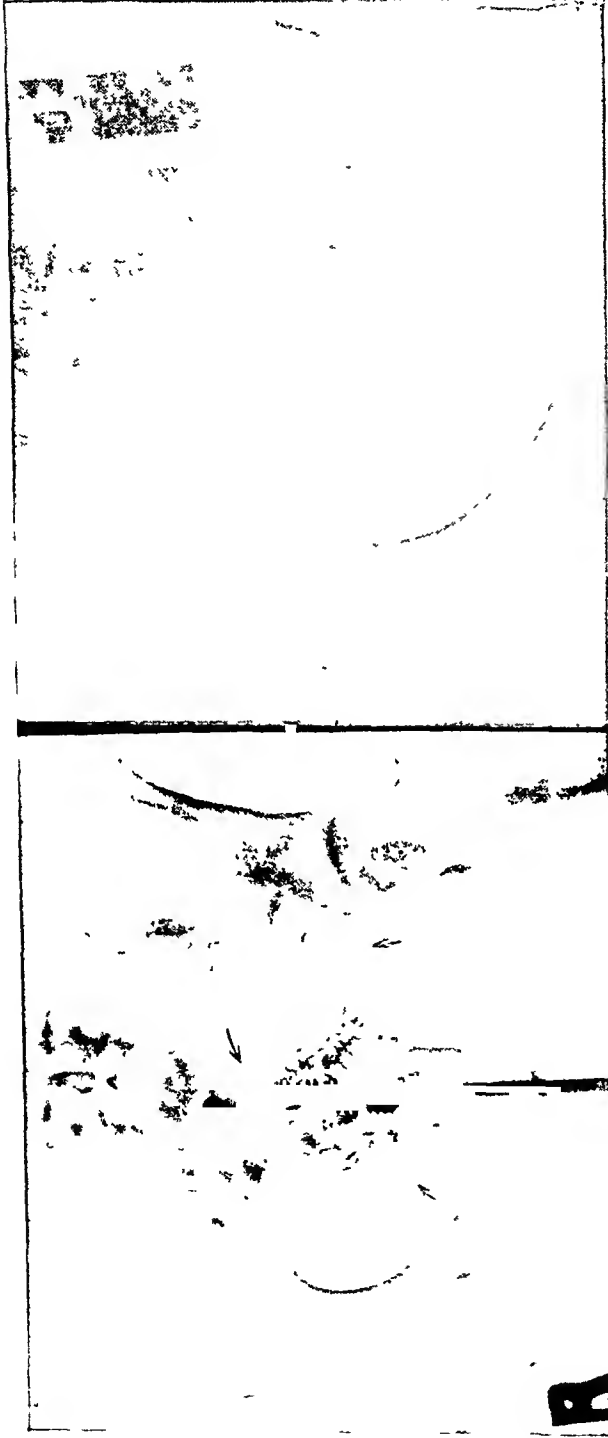
FIG. 4.

A film demonstrating a possible "pitfall" in diagnosis. The appearances suggest a fibroid, consistent with the clinical record, but operation failed to confirm this. Leakage of lipiodol into the pelvic veins is not necessarily productive of symptoms and probably occurs more often than is realized Lipiodol or air embolism is a potential danger, however, in all cases.

Upper arrow indicates filling defect; lower arrows indicate lipiodol in pelvic veins.

L.S.
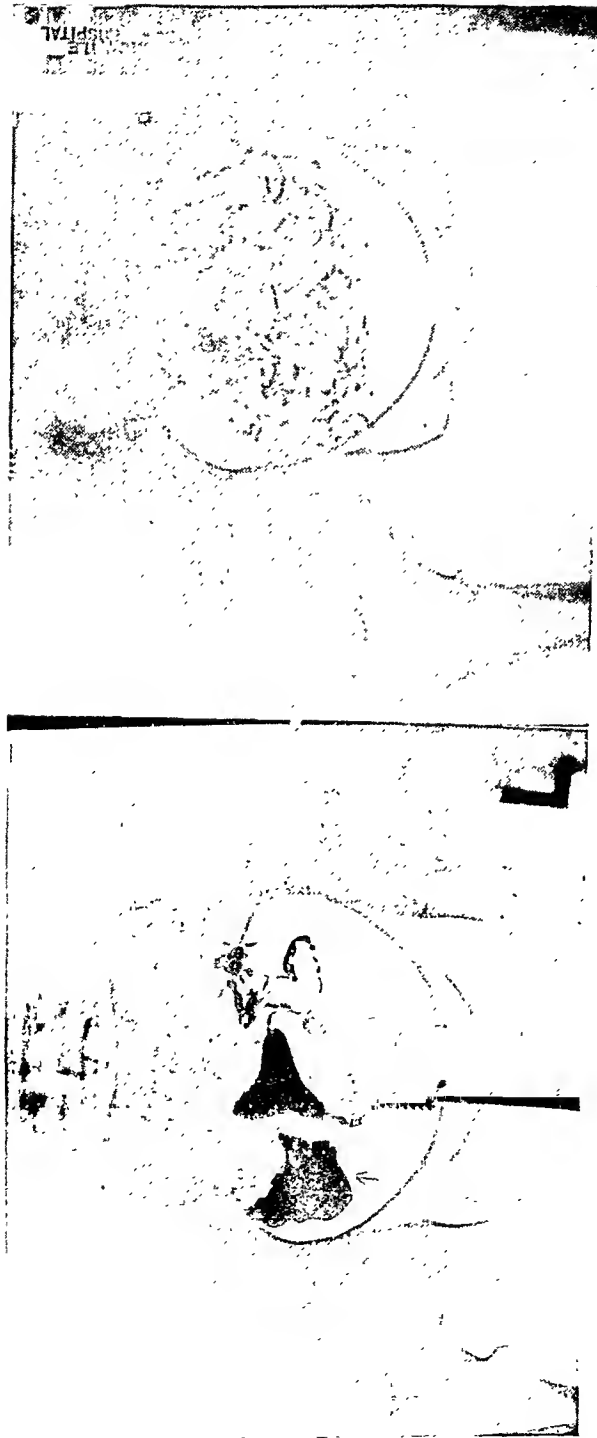
Fig. 5.

A normal hysterogram, indicating the value of a 24-hour film in distinguishing peritubal spill from hydrosalpinx (compare with Fig. 6).

L.S.
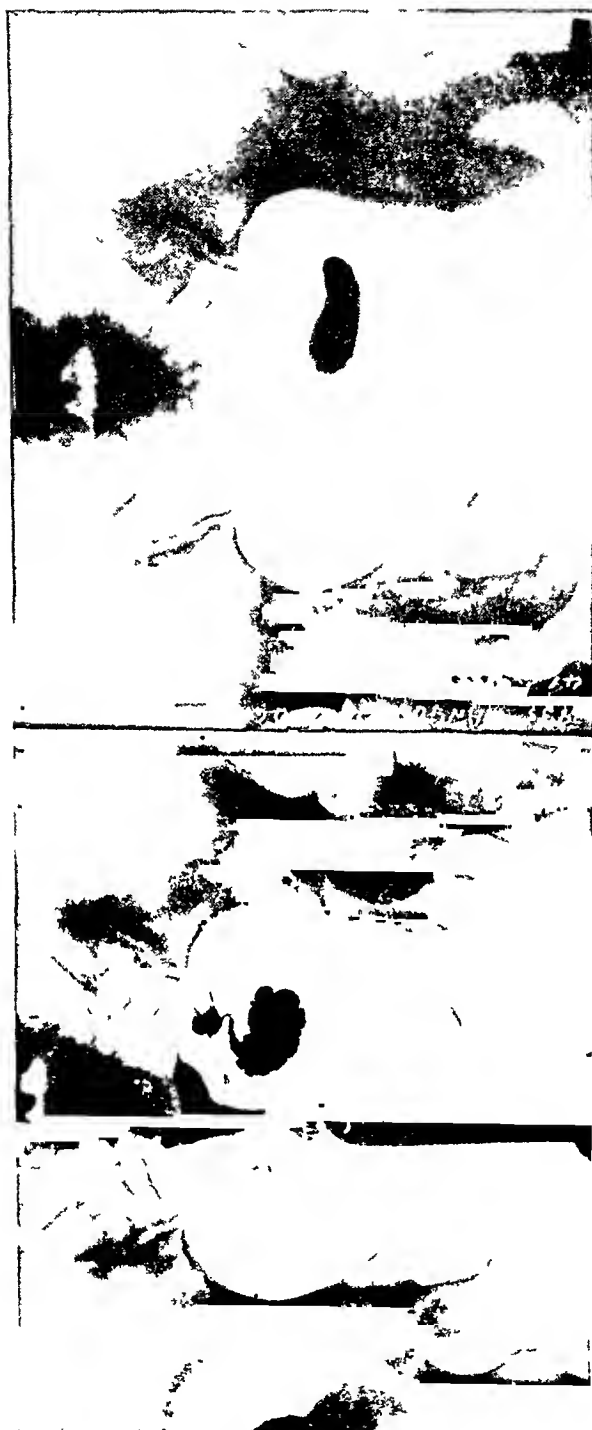
FIG 6.

Lipiodol-hysterogram showing non-patency, with a large hydrosalpinx on the left side

Fig. 7.

Occlusion of the Fallopian tubes prior to salpingostomy. The case was one
of endometriosis.

L.S.

FIG. 8.

Same case as shown in Fig. 7, after salpingostomy, indicating very free spill
Pregnancy occurred within 5 months of operation, after 8 years involuntary
infertility. Caesarean section was elective, in view of the age, infertility,
and presence of residual endometriosis in the rectovaginal septum
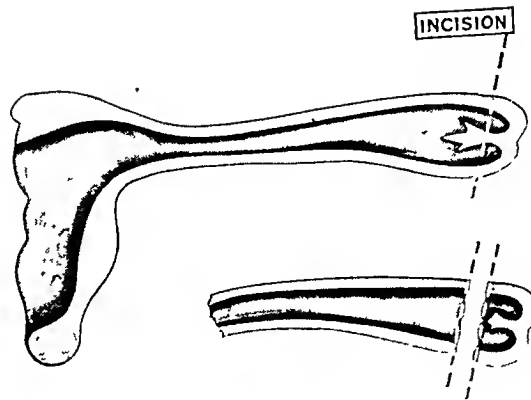
FIG. 9.

TRIANGULAR PIECE OF AMNION

PROBE
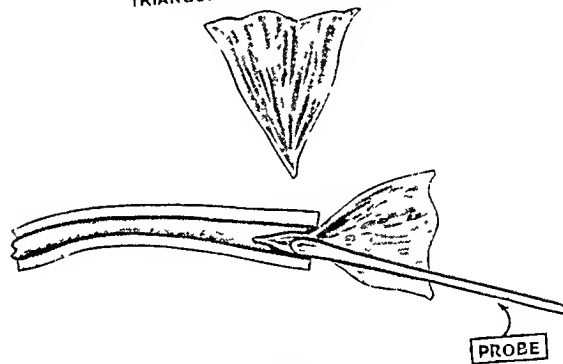
FIG. 10.

AMNION FOLDED BACK
OVER EDGE OF TUBE

3 PIECES OF
AMNION
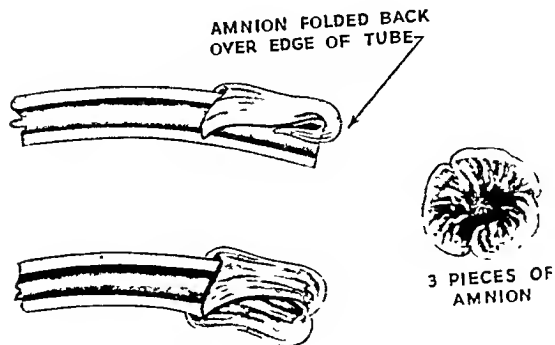
FIG. 11.

FIGS. 9, 10, 11.

Diagrammatic representation of stages in the treatment of tubal occlusion
by salpingostomy, using amniotic membrane.

with the aid of amnion prepared by the Department of Neurosurgery of that hospital, where it is used to prevent intracranial adhesions. The amnion is obtained from cases of Caesarean section in the Maternity Department, is washed in saline and separated from the chorion, soaked in 40 per cent saline for 12 hours, and sterilized by boiling for 1 hour, layers of amnion being placed between glass sheets. It is then preserved in absolute alcohol, a sample of each batch being tested for sterility.

Though I understand that this substance has been used by other workers without success, my own experience is that its use gives encouraging results in the form of tubal patency, for in every case except 1, in which follow-up by lipiodol has been permitted, free -patency has been established.

Technique.

The substance is friable and its proper application to the tube demands the use of very fine interrupted catgut sutures, considerable patience and a careful selection of case and planning of the shape of pieces of amnion to be used. Cases with fimbrial end occlusion are most hopeful, and those with rigid thickened tubes are usually rejected since function of the tube must be absent in such cases. The minimum of operative trauma must occur and additional surgery must be avoided, with the exception of Gilliam's correction of retroversion if present (Figs. 9, 10 and 11).

Results.

Using amnion, 21 cases have been dealt with. In most there was complete tubal occlusion and the operation was carried out to relieve this, but in a few cases the amnion was applied to tubes from which an ectopic pregnancy had been removed, or in which the primary reason for laparotomy was fibroids or other disease but occluded fimbrial ends of tubes were found at operation. Out of 21 cases, 14 have been followed up by lipiodol. In 13 of these full patency was demonstrated: in the remaining 1 only slight escape of lipiodol occurred. A further operation was carried out at the patient's wish, and patency demonstrated as a result, but without pregnancy to date.

Only 2 pregnancies are known to have occurred among these cases, but several were only recently dealt with and there is yet the possibility of a successful issue (Figs. 7 and 8).

Other methods of surgical treatment have been adopted in a few of the cases of occlusion coming under my care. The operation of implantation of the ovary into the uterus has been tried on 4 occasions without success but without ill-effects, and implantation has been attempted in 3 cases, with patency in 2, but without successful pregnancy. Unfortunately 1 of the last-named cases of patency was not traced in the most recent follow-up.

Conclusions and Personal Results.

Occlusion of the Fallopian tubes is an important cause of sterility. Attempts at treatment are justifiable in a high proportion of cases, and success is likely, though it cannot always be attributed to the treatment adopted, repeat insufflation being particularly uncertain in its real value. Major surgery is justifiable in a small proportion of cases, where fibroid tumours are associated with occlusion, or in certain types of intrinsic tubal disease, but in all cases full investigation is necessary, including that of the male, before surgery is undertaken.

Personal Experiences.

In a series of 800 cases of infertility, tubal occlusion is known to have been present in 130 and has been suspected in

many others. Of these cases 60 had complete occlusion. Pregnancy has occurred in 30 cases where there was indication of significant tubal occlusion, complete or partial: hormones played an important part in the treatment of 11 of these, and 3 were subjected to major surgery. Twenty women became pregnant after insufflation or lipiodol, combined with hormone therapy in some cases. Of all cases of sterility 28 per cent of the successful cures followed insufflation or lipiodol, though it is not certain that this procedure was responsible for success in all these cases.

Finally, in assessing results of the treatment of infertility due allowance must always be made for the effects of the lapse of time. Even Fallopian tubes which appear to be occluded on one occasion may become patent spontaneously and an attitude of reservation and even of reasonable scepticism is permissible when judging the results of any one form of treatment.

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The Histaminolytic Index of Blood during Pregnancy and its Clinical Application

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MARCOU and his colleagues (1938, 1939) were the first to describe the strong histaminolytic properties which blood acquires during labour. They found that the power to inactivate histamine which, according to them, is considerable even in normal blood, becomes greatly increased shortly before the delivery of the child. They suggested that this increase serves for the defence of the maternal organism against the imminent trauma of labour.

Subsequent observers (Werle and Effkemann, 1940; Zeller, 1941; Labhardt, 1941) confirmed and extended the observations of Marcou. It was found that an increase of histaminolysis could be detected as early as the third month of pregnancy and that the histaminolytic power continued to rise up to the seventh month. Anrep, Barsoum, Ibrahim, and Amin (1941) examined the blood of 92 non-pregnant and of 72 pregnant women. They failed to detect any histaminolysis in non-pregnant women, even though the incubation of the blood with histamine was prolonged to several hours. Histaminolysis appeared between the eighth and the tenth week of pregnancy, after which it progressively increased throughout the period of gestation, reaching a maximum towards term. The histaminolytic agent was present only in the plasma or serum, none being found in the red blood cells. After delivery, histaminolysis rapidly declined and disappeared in about 3 to 4 days. Ahlmark (1944) confirmed most of the above observations stating, however, that a trace of histaminolysis could be detected in the blood of non-pregnant women when it is incubated with histamine for as long as 22 hours. He finds that the maximal histamine inactivation occurs in the seventh month of pregnancy, after which it somewhat declines to rise again in the ninth month.

Ahlmark states that the rapid decline of histaminolysis postpartum begins after a period of a few hours, during which the histaminolysis rises above the level reached just before and during delivery. Anrep *et al.* (1941) failed to confirm this observation; according to them the decline, which begins about 8 hours after the delivery of the child, is not preceded by a temporary rise.

A further and more extensive series of observations was made by Anrep, Barsoum and Ibrahim (1947) on 150 non-pregnant and 136 pregnant women and on various laboratory and domestic animals. Their previous observations on the human subject were confirmed. It was also found that in animals there is no increase or only a negligible increase of histaminolysis during pregnancy.

The histaminolytic agent, which is probably identical with the histaminase of Best and McHenry (1930), is produced by the placenta from which it can be quantitatively extracted (Ahlmark, 1944; Anrep et al., 1947). According to Ahlmark, the histamine inactivation by the placenta per g. of tissue may be as much as 30 times greater than that of serum. Anrep et al. found it between 8 and 15 times greater. The latter authors also claimed that placentae at different stages of pregnancy yield approximately the same amount of the enzyme per g. of tissue, the total supply of the enzyme depending, therefore, on the mass of the placental tissue and not on some qualitative difference of it. The foetal blood also exerted some histaminolytic action which was, however, much inferior to that of the mother.

Histaminolysis is conveniently measured by an arbitrary histaminolytic index "HI" which is useful for comparative purposes but has no claim to any absolute value (Marcou et al., 1938). The "HI" expresses the percentage of histamine diphosphate destroyed by the blood, plasma, serum or tissue extracts when incubated for 30 minutes at 37°C. after addition of 3 µg of histamine diphosphate per ml. of the sample. A detailed description of a rapid and simple method for the determin-

ation of the "HI" is given at the end of this communication. The method, although the limit of its accuracy is about 10 per cent, is satisfactory for most clinical requirements.

The average "HI" for each month of pregnancy and for a few days postpartum is given in Table I.

TABLE I.

Average Histaminolytic Index for each Month of Normal Pregnancy and for a few days postpartum. The Index is measured in percentage of Histamine Diphosphate inactivated during 30 mins. at 37°C. by serum to which 3µg. of Histamine Diphosphate had been added per ml.

	Duration of pregnancy in months									Hours postpartum				
	1	2	.3	4	5	6	7	8	9	4–8	12–16	20–24	48	60
Number of estimations	22	21	15	18	14	19	23	19	66	19	12	14	12	15
Average "HI" per cent	0	9	30	47	60	67	76	85	92	92	75	45	18	traces

Between the 3rd and the 8th month of pregnancy the maximal deviations from the above averages usually did not exceed 10 per cent. Towards the end of gestation, that is in the 39th to 41st week of normal pregnancy the lowest index found for the serum was in 2 cases 80 per cent; in most it is about 95 per cent. Postpartum the diminution of the ."HI" is extremely rapid; in 24 hours the "HI" decreases to about half of the maximal value reached before parturition and in 48 hours to less than a quarter. Towards the end of the 3rd day, the "HI" is usually too small for quantitative determination. In 2 cases of normal pregnancy a weak histaminolytic action could be detected as late as the end of the 4th day after delivery.

THE HISTAMINOLYTIC INDEX IN ABORTION AND IN SUSPECTED FOETAL DEATH

Effkemann and Werle (1940a) observed that the histaminolytic power of the blood is diminished in cases of imminent and in-

complete abortion, as compared with that observed in normal pregnancy. Labhardt (1941), on the other hand, found in 9 abortions about the same degree of histaminolysis as in healthy pregnant women. Anrep *et al.* (1941) investigated 4 cases of imminent abortion, miscarriage and premature labour, one in the 5th month of pregnancy, 2 in the 7th month and 1 in the 9th month and found the " HI " conspicuously diminished below the values expected for these months. They suggest that the determination of the " HI " is of value for prognostic purposes. Ahlmark (1944) confirmed these observations in 4 cases of abortion which occurred during the 4th and 5th month of pregnancy.

The present series of observations comprises 26 cases of imminent abortion and miscarriage from accidental causes such as a fall or other injury. All cases brought to the hospital suffered from uterine bleeding which had started 18-36 hours before the collection of the blood sample. In most cases no surgical interference was necessary, the patient delivering the foetus either spontaneously or after a pituitrin course. The blood samples were collected within an hour or two after admission to the hospital and always before delivery took place. The results of the " HI " determinations are shown in Fig. 1.

It can be seen that in every case of threatened abortion or miscarriage the " HI " of the maternal serum was considerably below the value expected for the respective month of pregnancy. The degree of the diminution of the " HI " was of the same order as that observed 24 to 48 hours after the termination of normal pregnancy. In the 26 cases of the present series the " HI " was 54 to 100 per cent below normal, and the average diminution of the " HI " for all the cases was 78 per cent.

The rapid decline of the " HI " post partum and in cases of abortion suggests the possibility of using the histaminase reaction for a rapid detection of foetal death especially when it is accompanied by a separation of the placenta.

In this respect positive results could not be expected before the beginning of the 4th month of pregnancy, i.e., not before the " HI " had reached considerable values. Between the 4th and the 9th month of pregnancy the average " HI " rises from about 40 to about 90 per cent, so that a significant diminution of histaminolysis can hardly be missed. The histaminase reaction was investigated in the following 16 cases of suspected intrauterine foetal death.

Group A. Cases which Terminated in Foetal Death.

1. Multipara, 9 months pregnancy. Patient declared that all foetal movements had stopped 2 days before. Foetal heart sounds were inaudible. The " HI " was found to be 25 per cent instead of the expected 90 to 95 per cent. On the following day a dead child was delivered with signs that death had occurred 3 to 4 days before.

2. Multipara, 9 months pregnancy. Complained of abdominal pain which began after an accidental fall 18 hours before admission to the hospital. No movements of the child were felt for at least 14 hours. F.H.S. were inaudible. The " HI " of a blood sample collected immediately on arrival at the hospital was 65 per cent instead of 90 to 95 per cent. Twelve hours later the " HI " was 30 per cent and on the next day 15 per cent. The patient was treated by rupture of the membranes and application of an abdominal binder. A few hours after the last blood sample had been collected, the patient delivered a dead, non-macerated child 7 pounds in weight.

3. Multipara, 8.5 months pregnancy. Labour pains began a few hours before admission to the hospital. The patient reported that no movements of the foetus had been felt for 2 days. The abdomen of the patient was abnormally large which proved to be due to subacute hydramnios. F.H.S. were inaudible. The " HI " of the blood collected during delivery, was 50 per cent instead of 90 to 95

per cent. A few hours later the patient delivered an anencephalic, stillborn monster.

4. Multipara, 8 months pregnancy. Complained that the movements of the child had ceased for 4 days. Her "HI" was 35 per cent instead of 75 to 85 per cent. On the next day the patient delivered a macerated child.

dead child with a true knot of the cord was delivered on the 3rd day after admission to the hospital.

6. Multipara, 8 months pregnancy. Foetal movements ceased 10 days previously. There were no clinical signs indicating death of the child, such as regression of the breast or decrease of the

FIG. I.
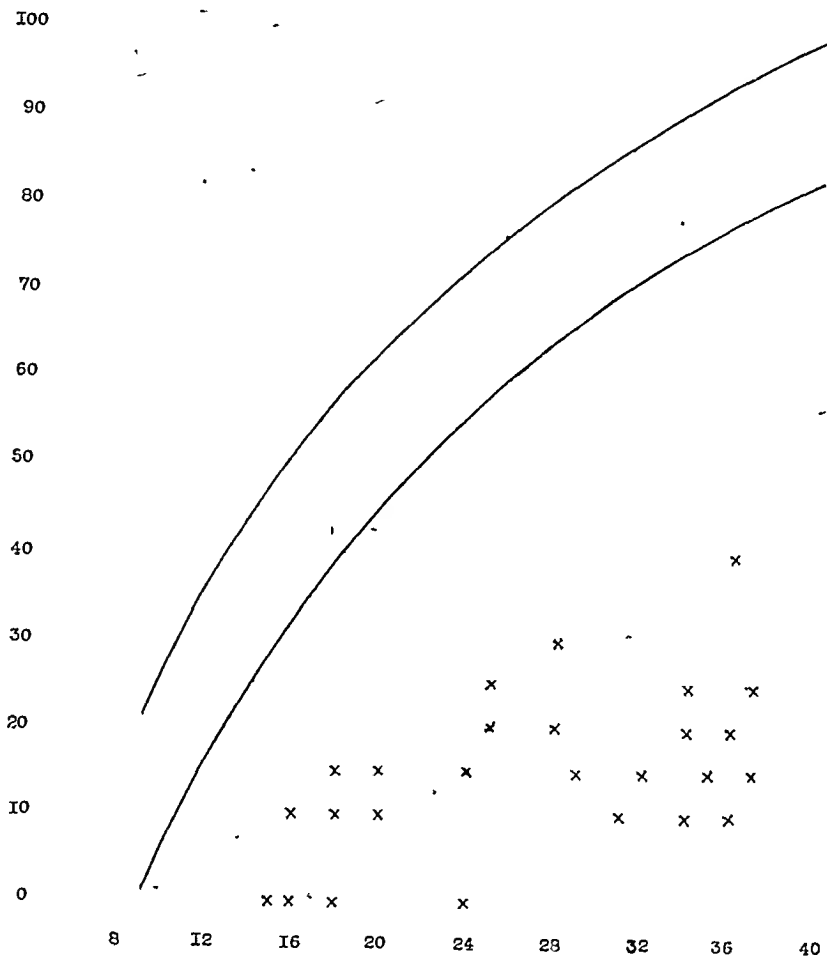
The two lines indicate the normal range of the "HI" in relation to the duration of pregnancy. The crosses indicate the "HI" found in 26 cases of imminent abortion or miscarriage resulting from accidental causes.

Abscissa, weeks of pregnancy; ordinate, "HI" in per cent.

5. Multipara, 8 months pregnancy. The child had ceased to move for 3 days; F.H.S. were inaudible. On the day of admission the "HI" was 40 per cent instead of 80 to 90 per cent. On the next day the "HI" was 15 per cent and on the 3rd day no histaminolysis could be detected. A

abdominal size. Clinically the abdomen corresponded to the 8th month of pregnancy. Foetal movements were not felt and the heart sounds were inaudible. The "HI" was 60 per cent instead of 80 to 90 per cent. On the next day the patient delivered a macerated foetus. The foetal head was

softened indicating that death had occurred at least 7 days before. Microscopically the placenta appeared to be normal although diminished in size (305 g.). Microscopically the different organs of the foetus (liver, spleen, kidney, etc.) and the umbilical cord, stained with haematoxylin and eosin, and after Levaditi, showed no evidence of syphilis or any other significant pathological change. Sections of the placenta revealed, however, a disseminated endarteritis obliterans of a moderate degree. This case belongs to those rare conditions, when the placenta survives the death of the foetus. The comparatively high " HI " observed 10 days after the cessation of foetal movements supports the conclusion made in our previous communication that the histaminolytic agent originates in the placenta and not in the foetus.

7. Multipara, 7 months pregnancy. Felt no movements of the child for the last 24 hours. Her " HI " was found to be 27 per cent instead of about 75 per cent. A dead child, without signs of maceration, was delivered on the same day.

8. Primipara, 6.5 months pregnancy. Complained that after an accidental fall 10 days previously all movements of the child had ceased. Her " HI " was zero instead of about 70 per cent. Three days later the patient delivered a macerated child.

9. Primipara, 6.5 months pregnancy. The patient had intercurrent eclampsia. She reported that movements of the foetus had not been felt for 24 hours. Her " HI " was found to be 20 per cent instead of the average of about 70 per cent. On the next day a stillborn child was delivered.

10. Multipara, 6 months pregnancy. No movements felt for the last 6 weeks following an attack of fever. The size of the uterus corresponded to 6th month of pregnancy. The Friedman test was positive. The " HI " determined on the day of admission to the hospital was between 10 per cent and 15 per cent instead of about 60 per cent. On inducing miscarriage the patient delivered a macerated foetus.

11. Multipara, early in the 6th month of pregnancy. Complained that for the last 2 weeks her abdomen and breasts gradually diminished in size. On examination the uterus was found to be harder than in normal pregnancy and to correspond in size to the 4th month. The " HI " was zero and the case proved to be a carneous mole.

12. Primipara, 4.5 months pregnancy. On the

day of admission the patient had a uterine bleeding which soon stopped and did not recur. The " HI " was below 20 per cent instead of about 50 per cent. The case ended by abortion on the same day.

Group B. Cases in which the foetus survived.

13. Multipara, 9th month pregnancy. Reported that the child had ceased all movements for 24 hours. F.H.S. were inaudible. The " HI " was 85 per cent. i.e., only slightly below the average for this month of pregnancy, i.e., 92 per cent. On the same day a living child was delivered. The child was 2 to 3 weeks premature.

14. A case of attempted suicide with an overdose of barbiturates. The patient was a primipara, in the 7th month of pregnancy. The mother was saved. The foetal movements, however, became very weak and then ceased completely. The F.H.S. became inaudible. The " HI " of the mother's blood, determined 24 and 36 hours after the accident was 55 and 65 per cent respectively instead of 70 to 80 per cent. The comparatively small diminution of the " HI," and especially the fact that it increased in the 2nd determination, allowed us to make a good prognosis. In fact, a day later, the heart sounds became again audible and the child began to move. At first the movements were very weak and infrequent, but soon they regained their normal character. Two months later the patient delivered a normal child.

15. Primipara, 6 months pregnancy. Foetal movements had not been felt for about 7 days. On admission, the patient said that she seemed to feel very weak movements, but was not sure. On examination no movements could be felt. On the day of admission the " HI " was 40 per cent but on the next day it rose to 52 per cent as compared with the average for the 6th month of pregnancy, i.e., 67 per cent. The comparatively high " HI " observed after 7 days of alleged cessation of foetal movements and especially the rise of the " HI " which occurred within 24 hours encouraged us to make a favourable prognosis. The condition of the patient rapidly improved and the foetal movements returned to normal. The pregnancy continued its normal course. A few days before labour the " HI " was 95 per cent. The patient delivered a normal child.

16. Multipara, 3.5 months pregnancy. Admitted on account of a small uterine bleeding. The " HI "

determined on the day of admission, was 30 per cent instead of about 35 per cent. This was considered to indicate that the placental circulation was not greatly affected. The bleeding stopped on the same day. The pregnancy continued and the patient ultimately delivered a normal child.

A comprehensive summary of the above 16 cases is given in Table II.

to the mother, no foetal movements could be felt for 10 days. As stated in the description of this case, the child most probably died slowly as the result of endarteritis obliterans of the placenta, which survived the death of the foetus. It is instructive to compare this case with

TABLE II.

Number of case	Duration of pregnancy in months	Duration of reported cessation of foetal movements	Expected "HI" per cent	Found "HI" per cent	Diminution of the "HI" per cent
GROUP A. *Cases which terminated by foetal death.*					
1	9	2 days	92	25	73
2	9	14 hours	92	65	30
,,		26 hours	92	15	84
3	8.5	2 days	89	50	46
4	8	4 days	85	35	59
5	8	3 days	85	40	53
,,		4 days	85	15	73
,,		5 days	85	0	100
6	8	10 days	85	60	30
7	7	24 hours	76	27	65
8	6.5	10 days	70	0	100
9	6.5	24 hours	70	20	71
10	6	6 weeks	65	10-15	77
11	5	—	60	0	100
12	4.5	—	53	20	62
GROUP B. *Cases in which the foetus survived.*					
13	9	24 hours	92	85	8
14	7	24 hours	76	55	28
,,		36 hours	76	65	15
15	6	7 days	67	40	38
,,		8 days	67	55	18
16	3.5	—	35	30	14

In 11 out of 12 cases which terminated by miscarriage, the "HI" of the mother's blood was conspicuously diminished below the average value expected for the month of pregnancy. The diminution ranged between 46 and 100 per cent. Case 6 showed only a moderate diminution of the "HI" in spite of the fact that, according

Case 8. In both, the movements of the child were reported to have ceased for 10 days, in Case 8 as the result of a trauma and a probable separation of the placenta and in Case 7 as a result of endarteritis without a separation. In Case 8 the "HI" diminished to zero while in Case 6 it remained as high as 60 per cent. In the 4 cases which

ended favourably the "HI" of the mother's blood was only slightly reduced below normal, between 8 and 18 per cent.

The limited material at our disposal does not permit of more than a guarded conclusion. It appears that a diminution of the "HI" by about 50 per cent or more below the value expected for the month of pregnancy indicates such a grave disturbance in the placental circulation as to be incompatible with a continuation of normal pregnancy. Especially unfavourable, in this respect, are those cases in which the "HI" progressively diminishes in the course of a few days or even hours. On the contrary, an increase of the "HI", as observed in Cases 14 and 15, is highly encouraging.

THE HISTAMINOLYTIC INDEX IN VARIOUS OTHER ABNORMALITIES OF GESTATION.

Toxaemia of pregnancy. In cases of pregnancy toxaemia the histaminolytic power of the blood is, according to Werle and Effkemann (1940b) and Zeller (1941) diminished, in comparison with that of healthy pregnant women. However, in a second communication Werle and Effkemann (1942) reported 12 cases of pregnancy toxaemia in which no deviation from the normal could be detected. Ahlmark (1944) examined 21 cases of albuminuria and toxaemia. In one-third of these cases the histaminolytic power was within normal limits, in one-third it was reduced to below the normal values, and in one-third it was increased above the normal. No correlation could be found between the degree of the symptoms and the histaminolytic power of the blood.

Our observations were made on 12 cases of severe eclampsia accompanied by albuminuria, hypertension and slight to moderate oedema of the face and of the extremities. The duration of the pregnancy varied between 35 and 41 weeks. In 8 cases

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the "HI" was within normal limits, in 4 cases it was reduced by not more than 20 per cent. So far we found no cases of eclampsia in which the "HI" was increased above the values observed in normal pregnancy (see method).

Extrauterine pregnancy. Werle and Effkemann (1940b) state that the usual increase of the histaminolytic power of the blood does not occur in extrauterine pregnancy, the blood behaving, in this respect, like that of non-pregnant women. On the other hand, according to Labhardt (1941) the diamine-oxidase reaction of the blood does not differ in extrauterine pregnancy from that of normal pregnancy. In a single case of extrauterine pregnancy observed by Ahlmark (1944) the histaminolytic power of the plasma was, up to the end of the 3rd month, almost normal. It failed, however, to increase any further so that after 16 weeks of pregnancy the histaminolysis was about 50 per cent below the expected result. The perforation of the tube took place a few days later.

Our observations, made on 3 cases of extrauterine pregnancy, confirm the findings of Ahlmark.

The first case, a primipara, was 5.5 months pregnant. She arrived at the hospital complaining of severe abdominal pain which had begun about 2 hours before. There was a small bleeding from the uterus. The examination revealed an extrauterine pregnancy with a probable perforation of the tube.

The "HI" of the blood sample, collected about 3 hours after the beginning of the acute symptoms, was 35 per cent instead of the average for this month of pregnancy of 60 to 70 per cent. The operation confirmed the diagnosis. The tube was considerably thickened and ruptured. The appearance and weight of the foetus corresponded to the 5th month of pregnancy but the placenta was much

smaller than normal, weighing only 68 g. instead of about 200 g.

The histaminolytic power of this small placenta was found to be, per g. of tissue, of the same order as that observed for normal placentae. It follows, that the placenta of extrauterine pregnancy presents, in this respect, no abnormality except that it is diminished in size. This observation lends support to our previous conclusion that the histaminolytic agent of the blood originates in the placenta and that the abnormally low " HI " of the maternal blood in extrauterine pregnancy is, most probably, due to the arrested development of the placenta. In this particular case the " HI " of the mother and the weight of the placenta roughly corresponded to the 4th month of pregnancy.

The 2nd case, a multipara, was 5 months pregnant. From the end of the 2nd month of pregnancy the patient had a slight bleeding which continued during the 3rd and 4th month. In the beginning of the 5th month the " HI " was 38 per cent. i.e., at the lowest level observed at this stage of pregnancy. Three weeks later, when 5 months pregnant, the patient entered the hospital with severe abdominal pain and some bleeding. The " HI " of the blood sample, collected about 2 hours after the onset of the acute symptoms, was 35 per cent. In other words, it had not increased since the last determination. In normal pregnancy the " HI " should have reached 50 to 60 per cent. The operation revealed an extrauterine pregnancy and a ruptured tube. The weight of the placenta was 82 g.

The 3rd case was similar to the 2nd. The patient, a multipara pregnant 18 weeks, first presented herself to the hospital on account of a minor non-gynaecological complaint. Her " HI " was 35 per cent, which is the lowest limit for this month of pregnancy. In a 2nd examination of the blood, made 3 weeks later, the " HI " was

found to be 32 per cent in one determination and 35 per cent in another instead of 44 to 55 per cent. After another 3 weeks, when 24 weeks pregnant, the patient was brought to the hospital with severe abdominal pain which had begun about 2 hours before. The case was diagnosed as an extrauterine pregnancy with a probable rupture of the tube. The " HI " of the patient was found to be 35 per cent and 38 per cent in 2 independent determinations instead of 57 to 73 per cent. The operation performed on the same day confirmed the diagnosis. On the next day, 24 hours later, the " HI " of the patient was about 10 per cent.

The placenta of this case weighed 78 g. and its extract had, per g. of tissue, approximately the same power to inactivate histamine as extracts of normal placenta.

The above cases of extrauterine pregnancy present a similarity in that in none did the " HI " rise above an average of 35 per cent which corresponds to about the 16th week of normal pregnancy. The placentae weighed 68 g., 82 g. and 78 g. respectively which, according to Ballantyne (1902) is the average weight of the organ for about the 17th week of gestation.

Our observations confirm the conclusions reached by Ahlmark. The increase of the " HI " in extrauterine pregnancy is at first approximately normal. As the pregnancy progresses the increase of the " HI " begins to fall behind the expected results and finally stops altogether. We suggest that the retarded increase of the histaminolytic power of the blood in extrauterine pregnancy is due to the arrested development of the placenta.

Placenta praevia. The " HI " determined during the 1st stage of labour in 2 cases of placenta praevia was found to be normal, 92 per cent and 95 per cent respectively.

Hydatidiform mole: Labhart (1941) observed an increase in the diamine oxidase reaction in case of hydatidiform mole. Ahlmark reports a case in which the power of the blood to inactivate histamine was increased from an average of 0.005 μg. per ml. per hour to a maximum of 0.15 μg. per ml. per hour which corresponds to an "HI" of about 7 per cent. A histaminolysis of this magnitude is too small to be detected with certainty by the method used in this communication.

In 5 cases of hydatidiform mole which came under our observation the histaminolytic action of the blood did not differ *from that of non-pregnant women.* In other words, within the limits of accuracy of the method, no histaminolysis could be detected, even when the incubation of the blood with histamine diphosphate was prolonged to 2 hours. Two of the cases were very advanced, the size of the uterus approximately corresponding to the 7th month of pregnancy although one woman claimed to be pregnant for 10 and the other for 14 weeks.

A further important observation was made by the determination of the histaminolytic action of the mole itself. In contrast with normal placental tissue, extracts of the mole have no power or a very limited power to inactivate histamine. Considering that the histaminolytic action of the placenta is up to 15 times stronger than that of blood in the 9th month of pregnancy, the difference between the mole and the normal placenta is highly significant. The absence or the extreme weakness of the histaminolysis in cases of hydatidiform mole acquires a special interest if one remembers that the gonadotrophic reaction of the urine, as measured by the Aschheim-Zondek or Friedman method, is in such cases extremely positive. In the 5 cases investigated by us Friedman's test was positive in a dilution of 1 : 50 to 1 : 100.

Chorionepithelioma. No reports could be found in the literature concerning histaminolysis in chorionepithelioma. In the 2 advanced cases observed by us the histaminolytic reaction was unmistakably positive, ranging between an "HI" of 20 and 35 per cent.

The 1st patient, a multipara 25 years old, had been treated in the hospital for a hydatidiform mole. Her blood was at that time examined and no histaminolysis could be detected. The patient was discharged from the hospital after all bleeding had stopped and after the Friedman test had become negative. About 3 months later the *patient returned to the hospital complaining* of persistent and irregular uterine bleeding. As a result of the examination of the patient, which included a microscopical examination of the scrapings from the cavity of the uterus, the case was diagnosed as a chorionepithelioma complicated by multiple metastases in the lungs. The Friedman test was intensely positive. Two blood samples were collected from the patient before the operation and one sample on the second day after the operation. The "HI" of these samples was 28 per cent, 32 per cent and 20 per cent respectively. The patient was extremely weak and exhausted. She died 3 days after the operation.

The 2nd patient, a multipara 35 years old, had an abortion in the 7th month of pregnancy following a severe trauma. She presented herself to the hospital about 6 months later complaining of uterine bleeding which lately greatly increased in volume. Examination of the uterine scrapings revealed a chorionepithelioma. The Friedman test was positive in a dilution of 1 in 100 and her "HI" in 2 consecutive examinations was found to be 30 per cent and 35 per cent. The patient was treated by total hysterectomy and deep X-ray therapy. Blood samples collected

3 and 4 days after the operation had no power to inactivate histamine. This patient recovered and was discharged from the hospital as cured.

DISCUSSION.

The fact that the blood serum acquires strong histaminolytic properties during pregnancy can be considered as well established. So far no other normal or pathological condition has been found which is accompanied by a similar histaminolytic reaction of the blood. Using the method described in this communication no histaminolysis could be found in the blood of men and non-pregnant women and the early claim by Marcou et al. (1938) that considerable histaminolysis can be detected in normal human blood must be definitely rejected. Ahlmark's statement (1944) that normal human blood inactivated histamine at the rate of 0.005 mg. per ml. per hour is open to considerable doubt since the biological methods used by him as well as by us are not sufficiently accurate to disclose such a small degree of histamine inactivation. A histaminolysis of such low intensity, even if present, is unlikely to be of physiological importance.

The increase of histaminolysis during pregnancy is absent or negligible in animals so that in the present state of our knowledge, it must be considered as peculiar to the human race.

Haemohistaminolysis can be first detected in the 7th to 9th week following the last menstruation, after which it progressively increases throughout the period of gestation. According to our observation Anrep et al (1941) it reaches a maximum towards the end of pregnancy; according to Ahlmark (1944) the maximum is reached during the 7th month after which histaminolysis somewhat declines to rise again in the 9th month.

Histaminolysis is such a typical and constant aspect of human pregnancy that it is of obvious importance to study this reaction in various abnormalities of gestation and to compare it with other manifestations of pregnancy such as the production and excretion of oestrogenic and gonadotrophic hormones.

The Aschheim-Zondek and Friedman tests are similar to the histaminolytic test in that no usual laboratory animal shows a significant increase of histaminolysis during pregnancy and none, with the exception of the anthropoid apes (and possibly the mare) gives a positive test for the chorionic gonadotrophin. On the other hand the curve of excretion of the gonadotrophin is quite unlike that of the increase of histaminolysis. The first reaches a maximum on the 50th to 60th day of pregnancy and then falls, during the next 20 days or so, to a much lower level, which it maintains during the rest of pregnancy; the 2nd progressively rises throughout the period of gestation. The Aschheim-Zondek reaction remains positive until 5 to 7 days after the birth of a full term child, while the disappearance of histaminolysis is much more rapid. There is a similarity between the histaminolysis and excretion of the oestrogens. Both appear in the 3rd month of pregnancy, reach a maximum towards the end of pregnancy and rapidly fall to a very low level in about 48 hours after labour.

The observations described in this communication suggest that a diminution of the histamine inactivating power of the serum during pregnancy indicates some grave abnormality of the placenta, e.g., a separation of the placenta, an arrest of its development, as in cases of extrauterine pregnancy, or its degeneration to a carneous or hydatidiform mole as already suggested by us in 1941. The extent of the diminution of the histaminase reaction can be used for prognostic purposes in cases of suspected

foetal death. The histaminase test is much simpler than the Friedman test. It is more rapidly performed and it gives results which lend themselves to a quantitative interpretation.

An interesting contrast is disclosed when the histaminase and the gonadotrophin tests are compared in hydatidiform mole and chorionepithelioma. The Aschheim-Zondek and Friedman tests are intensely positive in both. On the other hand, the histaminase test is negative in the mole and comparatively weak in chorionepithelioma. This seems to indicate that the histaminolytic agent and the chorionic gonadotrophins are produced by different cellular elements of the placenta.

As regards extrauterine pregnancy the Friedman test shows no definite change while the histaminase reaction begins to lag behind the normal curve at a fairly early stage of gestation and then ceases to increase altogether. It is of interest that per gram of tissue the diminutive placenta of extrauterine pregnancy yields the same amount of the histamine inactivating agent as normal placentae. The diminished histamine reaction of the serum is, therefore, probably due to the arrested development of the placenta.

The material presented in this communication has been gradually collected during the course of 6 years and only well controlled cases have been reported. In spite of this we are conscious of the fact that our material is limited and that, therefore, the results obtained cannot be considered as final. We hope that the observations described here will stimulate further research and that in the future determination of the histaminolytic power of the blood by means of the methods recommended by us or by any other method will be accepted as a routine test to be applied in any suspected abnormality of pregnancy.

Simplified method of the " HI " determination suitable for clinical purposes.

A few ml. of blood are collected from the cubital vein and allowed to clot in a test tube. Care must be taken that no alcohol or other disinfectants are present in the syringe. If the latter has been kept in alcohol, it should be first washed with normal saline. The blood serum can be used at once or kept overnight in cold storage. For the " HI " determination, 0.9 ml. of the serum or any multiple of this amount up to 4.5 ml. are warmed to 37° C. A solution of 30 μg. of histamine diphosphate in 1 ml. of Tyrode's solution is added in proportion of 0.1 ml. to each 0.9 ml. of the sample and the mixture is incubated for 30 minutes at 37° C. The sample is then rapidly diluted with Tyrode's solution using 5 ml. for each 0.9 ml. of the serum and at once heated on a flame to 80° to 85° C. It is not necessary to measure the temperature of the mixture since at the required moment the colour of the sample changes from light pink to a cloudy grey. After cooling, the sample is assayed on the isolated ileum of the guinea pig against a standard solution containing 0.5 μg. of histamine diphosphate. The guinea pig's ileum is suspended in an atropinized (10^{-7}) Tyrode's solution in a bath of 5 ml. capacity.

It has been shown in a previous communication that the assays with this method are accurate to about 10 per cent. The entire determination takes about 45 minutes. For most purposes a standard concentration of histamine diphosphate can be prepared in Tyrode's solution. For more accurate work, especially for sera of animals, it is advisable to prepare the standard solution in a diluted serum to which 0.5 μg. of histamine diphosphate per ml. is added *after* heating the diluted serum to above 80° C.

It is obvious that Barsoum and

Gaddum's method (1935) in which the histamine is extracted with trichloroacetic acid can also be used. The method is, however, time-consuming and presents no special advantage. When histaminolysis is studied in whole blood trichloroacetic acid must be used.

The determination of the histamine content of human serum before the addition of histamine is not necessary since it is too small to affect the results.

. The simplified method presents 2 disadvantages which are, however, unimportant for clinical purposes. ·

When the histaminolytic activity of the serum is very weak, the incubation period of 30 minutes may not be sufficient to disclose a measurable degree of histaminolysis. This can be remedied by prolongation of the incubation to 1 hour or more.

On the other hand, when histaminolysis is strong, the destruction of the histamine may be almost complete within a shorter time than the usual 30 minutes period of incubation. This can be remedied either by shortening the period of incubation or by increasing the initial concentration of histamine diphosphate in the solution in relation to the amount of the serum.

From the clinical point of view, we consider the second source of error as being of minor importance. As far as the histaminolysis of the serum is concerned, a "HI" above 90 to 95 per cent presents no special interest since it demonstrates nothing more than a normal condition. The greatest interest is presented by the cases in which the "HI" falls below the expected results.

It must be remembered that the "HI" is an arbitary unit, useful for clinical purposes but without a claim to an absolute value. When a more accurate estimation of a very low or a very high histaminolytic activity is desired the more complicated and time-consuming method devised by Ahlmark (1944) should be used.

The histaminolysis of placental extracts is so strong that special precautions have to be taken for its determination. In our work the placental extracts were prepared as described in another communication (Anrep, Barsoum and Ibrahim, 1947). The weight of placental tissue used for the incubation varied between 20 and 100mg. This enabled us to determine the amount of tissue which destroys histamine at the same rate as 1 ml. of a 9 months' pregnancy serum. The histaminolytic action of the placenta was then calculated per g. of tissue and compared with that of the serum.

SUMMARY.

1. The histaminolytic power of the serum, in cases of imminent abortion or miscarriage resulting from trauma or other accidental injury, is considerably reduced as compared with that expected for the given month of pregnancy. The extent of this diminution, in blood samples collected 18 to 36 hours after the beginning of the uterine bleeding, ranged between 54 per cent and 100 per cent with an average for 26 cases of 78 per cent.

2. In suspected intrauterine death of the foetus the histaminase reaction is useful as an aid in the prognosis of the outcome of the case. A diminution of the histaminolytic index to about a half or less than that expected for the month of pregnancy indicates such a considerable disturbance of the placental circulation as to render the normal continuation of pregnancy unlikely. Especially unfavourable are those cases in which the power of the serum to inactivate histamine progressively diminishes in the course of a few days or even hours. A diminution of the index by less than 40 per cent of the expected results, especially when it shows a tendency to increase in the course of a few days, is in favour of a good prognosis.

3. In severe toxaemia of pregnancy the histaminolytic power of the serum does not, as a rule, differ from that of normal pregnancy. In 8 cases the index was found to be within normal limits and in 4 it was reduced by not more than 20 per cent.

4. In extrauterine pregnancy the increase of the histaminase reaction is at first approximately normal. As the pregnancy continues the increase in the power to inactivate histamine becomes less conconspicuous than in normal pregnancy and finally stops altogether. At the time of the rupture of the tube the histaminolytic index was in 3 cases of extrauterine pregnancy about half of the expected value.

Extracts of the placenta of extrauterine pregnancy have approximately the same histaminolytic action per g. of tissue as extracts of normal placentae. It is suggested that the diminished histaminolysis of the serum in extrauterine pregnancy is due to the arrested development of the placenta.

5. In cases of placenta praevia the histaminolytic power of the serum is normal.

6. In 5 cases of advanced hydatidiform mole no histaminolysis could be detected by the method used in this communication. No evidence could be found that extracts of the mole have a power to inactivate histamine.

7. In 2 cases of chorionepithelioma, one following a hydatidiform mole and the other following abortion, the histaminolytic power of the serum was 28 to 35 per cent. No conclusions could be made in the 1st

case from the examination of the blood after the operation since she had profuse multiple metastases and died 3 days later. In the 2nd case, the histaminase reaction became negative 2 days after panhysterectomy.

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The Manchester Operation for Genital Prolapse

BY

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IN the April number of this Journal there is an article by Brentnall on Fothergill's colporrhaphy (Brentnall, 1947) in which he seeks to do honour to his old teacher. All the old colleagues and pupils of Fothergill would wish to join in this but, unfortunately, in honouring Fothergill, Brentnall has thought it necessary to belittle Donald and to devote several pages to descriptions of old vaginal operations in order to refute a claim which apparently he thought I and others had made of Donald being the first to do vaginal operations for the cure of genital prolapse.

In my first and second papers on this subject (Shaw, 1930, 1933) I mention all the operators he describes, and others, even including Dr. Marshall Hall and Mr. Hemming (of Manchester Square), although Brentnall says: " I can find no reference in the literature to it for thirty years."

As Brentnall was mortally stricken at the time his paper was written I hesitate to write to refute it, but for the sake of historical accuracy it is necessary to publish a short note.

For the early history of operations upon this condition I cannot do better than quote what I wrote in my second paper (Shaw, 1933):

" . . . Marshall Hall of London seems to have been the first to suggest narrowing of the vagina, but there is no record that he performed the operation himself. Heming in 1831 operated upon the anterior vaginal wall and was followed by Kilian, Marion Sims, Emmett, Savage, Aveling, Morton and Gaillard, Thomas, etc., all with various modifications and each claiming fairly good results.

" Now, when operations are more or less standardized so that it is necessary to quote large numbers to prove that one method is superior to another, it is only by reading the records of these earlier operators, written by themselves, that we can in any way realize the amount of original thought, manual dexterity and self-confidence which each advancing step required.

" Marion Sims's description of his first anterior colporrhaphy is a striking illustration as, in order to cure the prolapse, he was quite prepared to risk the production of a large vesico-vaginal fistula and to trust to his own ability to close this at a later stage. By sheer good luck this was avoided and an operation devised which could be performed by disciples with less skill and confidence.

" Operations upon the posterior vaginal wall and perineum were performed by Hegar, Simon, Emmett, Martin, etc., and the cervix was amputated by Huguier, Coupil, Sims, etc., but no one seems to have combined these three operations until some members of the Staff of the Women's Hospital attached to the University of Berlin and Donald of Manchester independently began to do so in 1888.

" Marion Sims, in the 1886 edition of his celebrated book, states that for the treatment of prolapsus uteri there are three surgical processes from which to choose. (1) Amputation of the cervix, (2) perineal operations, or (3) narrowing of the vagina by the trowel or triangular-shaped denudation of its anterior wall as performed by Emmett and himself; while the 1890 edition of Hart and Barbour contains this statement about perineorrhaphy: ' These operations help at least by enabling the patient to wear a ring pessary ', and that apparently was the object for which the operation was performed.

"In 1888 Cohen published the results of 105 cases of prolapsus uteri treated by colporrhaphy by Olshausen and Carl Schröder. In some of these cases only anterior, in others only posterior, colporrhaphy was performed, but in a few these two operations were combined. Of the whole series he claimed 56 per cent of cures, but he had 2 fatal cases.

"In this same year, 1888, my old chief, Donald of Manchester commenced, quite independently, to treat these cases by the combined operation of anterior and posterior colporrhaphy and amputation of the cervix."

The only correction I would make in this short history is that careful re-reading of Hegar's "Cyclopaedia", published in 1889, shows that he was doing an anterior as well as a posterior colporrhaphy.

It is quite clear from the above that I never claimed more for Donald than that he developed this operation at the same time as the Germans, nor would he have claimed more himself, as he frequently spoke to me of these German co-workers in the same field. What I claim for Donald is that he was the first man in England to combine anterior and posterior colporrhaphy with amputation of the cervix, to use it regularly for the cure of genital prolapse and so successfully, that by the time I became a resident at St. Mary's Hospital, in 1904, his seniors as well as juniors on the Honorary Staff were all performing a similar operation—surely the greatest triumph for any operator. Unfortunately Donald was very shy about writing. He had a feeling that it was a form of self-advertisement and thought that most of those who indulged in it did so in inverse ratio to their clinical experience. He did, however, prove that this was the one method of treatment for this particular condition. He convinced his colleagues, senior and junior, he taught his residents, and he was visited regularly by other operators from outside centres. In this way he felt he was spreading the gospel more surely than by writing.

For a short period he sometimes combined ventro-fixation with the double colporrhaphy, but he had passed this stage before I became a resident at St. Mary's, and during the four and a half years in which I held this office, 1904 to 1908, I did not see a single case of genital prolapse treated otherwise than by colporrhaphy except by two members of the staff of the Southern Hospital which amalgamated with St. Mary's in 1906.

Donald began the operation by splitting the cervix and amputating both lips by wedge-shaped incisions. Having closed these he did the anterior colporrhaphy by marking out an oval area extending from just below the urethral orifice to a point fairly close to his cervical sutures. In the note published in 1908 there are some drawings which are not anything like the incision I remember him making, and it is difficult to understand how he allowed these drawings to be published. I see that they were done by Fothergill, who, I think, must have placed inadvertently the widest part of the incision much nearer to the urethra than Donald commonly placed it. The incision which Donald usually made is well illustrated in a paper published by Fothergill in 1915.

During the years of my residence Donald always laid great stress upon the suturing of deep tissues, and though he did not give them anatomical names he took a good bite of the tissue on each side of the cervix and tied them together in front of the cervix. In his second paper (Donald, 1921) he remarks that in the first one he had ceased to use buried sutures for a short period, but he quickly returned to this method.

In posterior colporrhaphy he began with the apex near the cervix and the base of the perineum, and here again he relied for

a good result upon the deep suturing rather than on the superficial skin sutures.

In 1906, on the amalgamation of St. Mary's with the Southern Hospital, Fothergill joined the staff as an Assistant Surgeon, without beds, of the latter hospital. Fothergill had a well-trained scientific mind, expressed himself well both in speech and in writing. He quickly realized, as did neither of his two senior Southern colleagues, what good results were being obtained by the use of this combined operation for genital prolapse, and his scientifically-trained mind impelled him to search further into the subject for the reason. In 1907 he read a paper before the Royal Society of Medicine on "The Supports of the Pelvic Viscera; a review of pelvic anatomy with a clinical introduction". (Fothergill, 1907).

Several people had been writing about the supports of the uterus, but this was the first time that it had been brought clearly and forcibly before a body of British gynaecologists. Fothergill expressed the opinion that the support of the uterus was the parametrium around the main uterine vessels, which spread also into the utero-sacral and utero-vesical folds. Apparently he did not believe that the pelvic muscles played a part, whereas now we consider both the muscle and the parametrium to be of equal importance. It is interesting to note that in the discussion after this meeting Paramore raised this particular point. Having had his interest in this subject aroused Fothergill sought to improve Donald's operation by modifying it in such a way that the parametrium was more completely exposed and therefore more easily sutured. He therefore made his incision for the anterior colporrhaphy triangular in shape with its base at the cervix. This modification is clearly shown in the paper written in 1915.

Later still (Fothergill, 1921) he extended the incision around the cervix from the angles at the base of the anterior colporrhaphy and so amputated the cervix along with the triangular flap of skin in the anterior vaginal wall. There is no special benefit in removing the skin and the cervix in one piece, but it was an improvement to amputate the cervix along the base of the anterior colporrhaphy, as one of the drawbacks to Donald's operation was the bridge of skin and sub-adjacent tissues left between the incisions of the anterior colporrhaphy and of the cervix.

Fothergill did a posterior colpo-perineorrhaphy in the same way as Donald, except that he preferred to dissect it from below upwards, whereas Donald always did it from above downwards.

That Fothergill's operation was merely a modification, with some improvements, of Donald's original one is clearly recognized by Fothergill himself. In 1921 he wrote:

" . . . When I came to Manchester in 1895 I found that, owing to the initiative of my senior colleague, Professor A. Donald, the surgical treatment of genital prolapse was already highly evolved and most efficient. The anterior colporrhaphy incisions were larger than those I had seen and the whole thickness of the vaginal wall was removed, not merely a superficial layer. Donald had also brilliantly combined the operation of posterior colporrhaphy and perineorrhaphy in a single operation done from above downwards. This was a great simplification and advance in the treatment of rectocele. For the last thirty years Donald has operated in hospital four days a week, and has cured an enormous number of cases of prolapse by amputation of the cervix, extensive anterior colporrhaphy and his own colpo-perineorrhaphy.

" My own contribution to the surgery of prolapse was made at a much later date. Clinical experience gradually taught me that the uterus, vagina and bladder were mainly kept in their places by the lateral combination of unstriped muscle and connective tissue known as the parametrium and the paracolpos. Finding that

several anatomists had come to the same conclusion, I brought their names and their work before the Royal Society of Medicine in December 1907. The facts then mentioned have been re-discovered subsequently with surprising frequency in various parts of the world. The practical application of this was that anterior colporrhaphy could best be improved by carrying the incision well up and out on either side of the cervix, fully exposing the paracolpos, so that closure of the wound must bring together in front of the cervix structures which were formerly at its sides. This modification of technique I advocated before the Edinburgh Obstetrical Society in 1908."

Fothergill's operation was a modification of the original operation done by Donald. He called attention to important anatomical facts and the shape of his anterior colporrhaphy allowed these deep structures to be sutured more freely. He himself did not bury any sutures, but relied upon the vaginal skin sutures being placed sufficiently deeply to pick up the important deep parts of the pelvic floor. This modification of the operation eliminated the redundant tissue left by Donald's operation between the cervical incision and the anterior colporrhaphy, and it also proved that the vagina need not be narrowed so much.

From the time when Donald first began to treat genital prolapse with this combined operation in 1888 this method has been carried out without a break by the members of the Honorary Staff at St Mary's Hospital. In various ways each has modified the operation, though each has adopted the general principle of anterior and posterior colporrhaphy with amputation of the cervix and tightening of the deep pelvic tissues. In detail we may seem to differ, in general principles we all agree.

In recent years many operators in various centres and many countries have written upon this subject, describing the modifications they have adopted, and sometimes their followers have attached

their names to the operation. This leads to confusion. When I lectured upon this subject in America (Shaw, 1933) it seemed too late to attach Donald's name to the operation, especially as he had never adequately described it in print, but it seemed unfair to attach to it the name of any subsequent operator who had merely modified the operation. Therefore rather than attach any individual operator's name I suggested that it was preferable to use one term to cover all such operations which include a double colporrhaphy with amputation of the cervix and suturing of the deep structures and, as the operation was developed in Manchester and has been continuously employed in that school for fifty-nine years, it seems reasonable to employ the generic term of " The Manchester Operation."

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Unsuspected Tuberculous Endometritis

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INTRODUCTION.

SINCE the middle of the eighteenth century there have been isolated accounts of tuberculosis involving the female genital tract, but the clinical significance of this syndrome was not appreciated until Louis' studies on phthisis had begun to influence medicine. In 1847 Kiwisch described a case in which there was tuberculosis of the corpus uteri, but for nearly 100 years after this such patients were regarded as pathological curiosities, and the presence of tubercles in the endometrium was always overshadowed by the concomitant gross salpingitis. It is only in recent years that Sutherland (1943) and others have reported the finding of tubercles in the endometrium of patients who on clinical examination present no evidence of infection in the Fallopian tubes or elsewhere.

The type of tuberculous endometritis with which this paper deals is that occurring in patients who are not obviously ill, but who complain of sterility or menstrual irregularity. On investigation they are not found to have any clinically detectable abnormality in the pelvis or elsewhere, yet histological examination reveals the presence of tubercles in the endometrium. It may appear that such grouping is arbitrary and it is very probable that many persons with similar conditions do not report to their doctor; furthermore, some patients who at first examination fail to show any tuberculous lesion in the pelvis, subsequently develop clinically detectable tuberculous salpingitis. However, the majority of patients presenting in the way described conform, as far as natural history is concerned, to a type. Therefore it would seem justifiable to give an account of a group of such cases which has been studied at Oxford during the past $8\frac{1}{2}$ years.

FREQUENCY.

It is difficult to be certain how rigidly the above criteria have been applied by other workers, but approximately similar groups of patients have been reported by Sutherland, who fully reviews the literature, Sharman (1944), Halbrecht (1946), Stockart and Ferin (1939), and Rabau, Halbrecht and Casper (1943). It is impossible to estimate the incidence of this type of lesion in the population as a whole, as the diagnosis can be made only by histological examination. The frequency might be expressed as the number of tuberculous cases per 100 patients whose curettings have been examined. This latter figure is difficult to ascertain, as patients of all kinds may have a number of repeated biopsies. Therefore, there remains the cumbersome ratio of

positive patients per 100 unselected curettings examined. Clearly the number of tuberculous curettings expressed as a percentage of all curettings will depend among other things, on the number of repeated curettings on each patient.

It would seem that Sutherland's figures are strictly comparable. Over a 7-year period he found that the gross incidence of tuberculous endometritis in 5,521 curettings examined for all purposes was 1.1 per cent (61 positive specimens). After subtracting from this last figure those cases who had clinical evidence of pelvic tuberculosis there remained in his series 49 positive specimens obtained from 33 patients. Expressing these figures as a percentage of the total number of unselected curettings, one finds that he has 0.89 positive curettings or 0.6 tuberculous patients per 100 patients so examined for all purposes. The incidence among patients complaining of sterility is much higher than in any other group. Thus, Sharman (1944) diagnosed 20 cases in a group of 390 infertile women in Glasgow, giving an incidence of 5.1 per cent. Halbrecht (1946) reported an incidence of 5.5 per cent of cases among 820 infertile patients in Tel Aviv.

During the last 8½ years (January 1938 to June 1946) we have examined 3,600 curettings for all purposes and found tuberculous endometritis in 37 curettings from patients who showed no clinical evidence of pelvic tuberculosis, giving an incidence of 1.03 per cent. These 37 curettings were obtained from 23 patients, giving an incidence of 0.59 tuberculous patients per 100 patients so examined; in surprisingly close agreement with Sutherland's figures of 0.6 per cent. Of these 3,600 curettings, 898 were obtained from patients whose primary complaint was sterility, and tuberculosis was present in 26 of these curettings. Thus 2.89 per cent of the curettings from the sterility group were infected. Of the 23 tuberculous women 17 complained of sterility, giving an incidence of 1.89 sterile patients per 100 curettings from the infertility clinic.

CLINICAL FINDINGS.

All 23 cases occurred in the reproductive age. The primary complaint of 6 of the cases was menstrual irregularity, and of these, 2 were single women. The remaining 17 complained of sterility, and 9 of these also suffered from menstrual disturbances. In none of the 23 had pregnancy occurred within 10 years of the date on which the diagnosis had been made nor has any pregnancy been reported to us in the follow-up of these cases. On the other hand, pregnancy has been reported in a number of cases of tuberculous salpingitis but this occurrence must be rare.

On clinical examination of the 23 patients, we found that all were living a normal life and enjoyed apparently good health. An X-ray of the chest showed no evidence of gross pulmonary tuberculosis in any case.

The results of urine-analysis and full blood-counts were within normal limits in every case. The blood sedimentation-rates were estimated in only 6 of the cases of this series. Three were below 10 millimetres in 1 hour, the remaining 3 were 16, 18 and 27 millimetres in 1 hour (Westergren) respectively.

In a few cases the diagnosis was suspected before the endometrial biopsy was examined because of a history of an old tuberculous lesion elsewhere in the body, or of a family history of tuberculosis. The suspicion was strengthened when, in addition, the patient complained of menstrual disturbances. But in all cases the diagnosis was finally established only by the histological examination of the endometrial biopsies.

The follow-up is summarized in the subjoined table. It is incomplete as a number of cases were lost sight of, and cannot now be traced.

Total number of cases	...	...	...			23
						Age in years
Oldest	...	...	...	...	...	50
Youngest	...	...	...	...	...	17
Average	...	...	...	...	...	33

Primary complaint :

					No. of patients
Sterility	...	...	...	...	...	17
Sterility only	...	...	...	...	8
Menorrhagia	...	...	...	...	5
Hypomenorrhoea	...	...	...	1

Secondary complaint :

Menorrhagia	...	...	...	...	6
Hypomenorrhoea	...	...	...	3

Tubal insufflation :

					No. of patients
Patent	...	...	...	...	...	5
Blocked	...	...	...	...	8
Not performed	...	...	...	...	10
Local extension following insufflation	.	. .	...	.	2

Follow-up :

Less than 3 months	...	...	...	6
Less than 1 year	...	...	...	5
Less than 3 years	...	...	...	6
More than 3 years	...	...	...	6
Remaining apparently well :				
No treatment	...	...	...	17
Local extension	...	...	...	5
Spontaneous ...	...	...	...	3
After tubal insufflation ...	...	2
Local extension : total hysterectomy, bilateral salpingo-oöphorectomy :				
now well ...	...	...	...	...	5
Miliary spread : death	...	...	...	1

Two patients have been under observation for 9 years, which is the longest follow-up in the series. The first, a single woman, originally attended complaining of periods of amenorrhoea and oligomenorrhoea. In time the menstrual cycle became normal but the endometrial biopsy is still

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* One of these 3 patients was diagnosed before June 1946. She subsequently developed a tubo-ovarian mass. She now feels well 2 months after radical clearing of the pelvis (1.3.47).

positive. The second married in 1933 and was in bed for 2 months in the same year with dry pleurisy. In 1938 she complained of sterility; a curetting showed tubercles in the endometrium. In 1947 she remains apparently well, but is still sterile and the curettings (not included in the figures of frequency) still show tubercles. There is strong presumptive evidence in this patient that the infection occurred in 1933 and has remained quiescent for 14 years. It will be seen that the majority of the women remain apparently well without treatment, although in 5 patients local spread occurred and in 1 miliary spread caused death.

The pelvic spread in 2 cases immediately followed tubal insufflation, performed as part of a routine investigation of sterility, before the diagnosis had been made. This has led us to refrain from testing tubal patency in cases in which tuberculous endometritis is suspected until the condition has been excluded by an endometrial biopsy. In all 5 cases in which there was local spread, radical clearing of the pelvis was undertaken and so far these cases have remained well. Contrary to expectation formation of fistula occurred only once. This fistula was excised and histology showed no evidence of tuberculosis.

The only patient who has died felt well when first seen and diagnosed. She did not accept the diagnosis and refused all further help. Months later she was admitted to hospital with a tuberculous pleural effusion and within a few weeks developed signs of meningitis and died. At a postmortem examination there was evidence of miliary spread. The only active tuberculous foci were in the endometrium and Fallopian tubes, although naked-eye appearances of these were strictly normal. There was, however, a calcified gland present in the messentery and, although this showed no sign of recent activity, it must be assumed to be the original focus.

TREATMENT.

The natural history of the condition is not sufficiently clear for us to be certain of the correct method of treatment and the main object of this paper is to record our observations on the cases we have seen, so that ultimately treatment shall be based on adequate knowledge of the disease.

All these patients with tuberculous endometritis were subjected to a thorough clinical examination, X-ray of the chest, full blood-examination and urine-analysis in an attempt to find a primary focus. Those who showed any sign of local spread, the earliest usually being a clinically enlarged Fallopian tube, were advised to have the whole uterus and both appendages removed, with the satisfactory results described above. Those who felt well were kept under observation. An X-ray of the chest, blood sedimentation-rate estimations, and endometrial biopsies were repeated when possible at 3 to 6-monthly intervals. Sanatorium treatment has not proved of any value in our series, as 3 patients who agreed to accept such treatment eventually developed local spread.

PATHOLOGY

The pathological material of this series consists of 35 tuberculous and 3 non-tuberculous curettings and 5 of the uteri removed, including the one removed at the post-mortem examination from the patient with miliary spread. Macroscopically the curettings had no characteristic features. The microscopic appearances in every case were similar to the interstitial form described by Jameson (1935) and did not differ significantly from the tuberculous process in other organs. The difficulty lies in the scarcity and small size of the lesions. Thus in 16 per cent of these specimens only one definite tubercle was found, sometimes only after thorough examination of serial sections; serial sections of 3 other specimens from these proved cases showed no evidence of the typical cellular reaction, and extensive sections of the endometrium of some of the uteri removed at operation showed only a very occasional tubercle. Great care must, therefore, be taken before concluding that even a series of negative curettings indicate the absence of a tuberculous process. In 1 case, 2 biopsies, taken 3 months apart, showed typical tubercles, after a 2-year interval a further 2 biopsies (1 after June 1946 and not included in the figures of frequency) were both negative on histological examination and culture; yet we still do not feel we have sufficient evidence to say that this patient has recovered.

The essential lesion is a small collection of epitheloid cells; these cells and the general pattern of the lesion are, with practice, fairly easy to distinguish even when the other criteria are absent. Frequently these cells fuse to form giant cells, especially in the larger lesions, but giant cells were absent in 38 per cent of the curettings. Incipient caseation was seen in only 6 per cent and tiny areas of fibrinoid necrosis rather more often. Gross caseation was not seen in any case in this series. If caseation is extensive the specimen will probably be found to come from a uterus with tuberculous myometritis, a rare but well-recognized condition not dealt with here. The cuff of small lymphocytes is usually present and is often the first abnormality to catch the eye, but was absent in 17 per cent of the specimens. Diffuse lymphocytosis, fibrosis and oedema were each present in about 50 per cent of the specimens.

Examination of the 6 uteri showed that in all cases the uterus appeared normal to the naked eye. The histology was similar to that of the curettings. The rarity of the

tubercles has been mentioned. The Fallopian tubes varied in size from one that, to the naked eye, was strictly normal, to a tubo-ovarian abscess 7.5 cm. in diameter, which had developed since the patient was originally seen, when no clinical abnormality of the pelvis had been recognized. The histological appearance of the Fallopian tubes varied from a frank, caseating, tuberculous process spreading into the muscle to a chronic inflammatory, proliferative and adhesive salpingitis with a few discrete tubercles in the sub-epithelial layers; but in every Fallopian tube examined, a tuberculous lesion was present. The ovaries were involved only when they became incorporated in a tubo-ovarian abscess.

CULTURE.

We have ground up the curettings and injected them into guinea-pigs and cultured them on Lowenstein's medium. Both procedures appear to be equally reliable. The results of culture are not encouraging as only 4 (28 per cent) out of a total of 14 grew *M. tuberculosis* and the type was reported as human in one. Yet culture should be undertaken in every case. In one case, which had repeatedly been positive, one specimen was halved. Serial sections of one half showed only one indefinite lymphoid aggregate, while *M. tuberculosis* was isolated by culture of the other half of the specimen.

There has been much speculation whether, at menstruation, all the tubercles are shed with the endometrium and reinfection takes place from the Fallopian tube, or a few tubercles remain in the basal layer of endometrium, and reinfect the next month's endometrium. All sections have been examined with this problem in view and the results do not confirm either hypothesis. The majority of the specimens were in the secretory phase, but curettings taken earlier in the month differed in no way from the positive secretory curettings. The depth of the tubercle in the endometrium could not often be determined but these sections suggest that tubercles exist throughout the thickness of the endometrium at all stages of the cycle.

Other cases of tuberculous endometritis may have been missed, particularly as it is not practical to cut serial sections of all curettings; it is only reasonable to undertake this additional labour when there is either a history of tuberculosis elsewhere in the body or, as more often occurs, inspection of the routine section shows either fibrosis, diffuse lymphocytosis or lymphoid aggregates. One case, not included in this series, was almost certainly incorrectly diagnosed as tuberculous. Two curettings showed lymphoid aggregates with slight diffuse chronic inflammatory cellular infiltration. In one of the lymphoid aggregates, an acid-alcohol-fast rod was seen. Hysterectomy was performed and sections taken from the cervix, uterus and Fallopian tubes showed evidence of a chronic inflammatory reaction but no epithelioid systems and the appearance in general was not that of tuberculosis. The foreign-body reaction of the uterus following injection of lipiodol, might also cause confusion.

It is reported by Roberts (1947) that the talc used on gloves may be introduced into the peritoneum during a laparotomy. It can get into the Fallopian tubes where it may cause a foreign-body giant-cell reaction, the pseudotuberculosis silicoticum of Shattock (1916); he does not mention the endometrium. It appears, therefore, that when there is a history of a previous laparotomy it would be wise to examine suspicious sections of the Fallopian tubes, and even sections of the endometrium, with crossed nicol prisms, when any doubly refractile particules will become visible.

CONCLUSIONS.

As the diagnosis can be made only on histological examination of curettings and the diagnostic tubercles may be rare, all the fragments of endometrium obtained at curettage should be examined as a routine. Serial sections should be taken through the block when there is a history of some other possible tuberculous lesion, or when initial examination shows diffuse lymphocytosis, lymphoid aggregates or fibrosis. Examination of such curettings should always include either culture or guinea-pig inoculation. Even in these suspicious cases it is probably unwise to perform total curettage in order to increase the chances of finding a diagnostic lesion because of the risk of spreading the infection *via* the blood-stream.

Examination of our sections did not help to resolve the question of whether the endometrium is reinfected each month from an occasional tubercle remaining in the basal layer which escapes being shed, or from the Fallopian tubes. In every case in which the tubes were examined histologically they were always found to be infected, thereby lending some support to the second hypothesis.

The diagnosis of tuberculous endometritis will sometimes be overlooked, unless pathologists and clinicians constantly bear the possibility in mind. When the diagnosis is made, we are still uncertain of the correct method of treatment. If it is believed that miliary spread in the fatal case arose from the endometrium then it might be justifiable to perform a total hysterectomy and bilateral salpingo-oöphorectomy on every case. On the other hand miliary spread appears to be rare, and normal health over long periods is common, therefore it is probably wiser to be watchful and conservative and to treat each case on its merits.

SUMMARY.

The gross incidence in Oxford of tuberculous endometritis in patients with no clinical abnormality of the pelvic organs or lungs for an $8\frac{1}{2}$-year period is 0.59 cases per 100 unselected curettings. The incidence in the sterile group alone is 1.89 per cent. Of the 23 cases observed, 17 remained apparently well while under observation; in 5 local spread occurred, which was treated by total hysterectomy and bilateral salpingo-oöphorectomy, and 1 case not submitted to operation died of miliary spread. The clinical course and pathology are described. The danger of spreading the disease by tubal insufflation and the rarity of the tubercles in some cases are emphasized. All suspected curettings should be cultured.

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Icterus in Pregnancy

A Clinico-Pathological Study including Liver-Biopsy

BY

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THE term " General Physiology of Gestation " has still an uncertain implication. Valuable contributions to this subject have been made but there yet remains the difficulty of correlating functional changes of one organ with those of another. Particularly is this true with an organ such as the liver whose functions are so varied. Some of the common liver-function tests give in pregnancy results which in a non-pregnant woman could only be considered as pathological. Examples of such variation can be seen in the decrease in oxidation-rate and detoxication-capacity, in the retention of certain intermediate products of metabolism and so forth (Heynemann, 1936; Neuweiler, 1939; Herold, 1939; Laqueur and Ovacik, 1946). Findings that might be accounted typical for all pregnant women do not exist since there is such a wide variation in the so-called normal limits in pregnancy.

The instability of the neuro-vegetative system (extra activity of the thyroid, changes in function of the posterior pituit-ary and adrenal cortex, multiplication of certain cells in the anterior pituitary) influences the validity and reliability of functional tests in pregnancy. It is difficult enough in the non-pregnant to agree on what should be considered "physiological" and what "pathological". How much more is this the case in pregnancy where the range of metabolic functions is so enlarged.

The problem in pregnancy is to decide whether certain changes are : (1) due simply to the condition of the pregnancy; (2) fortuitous incidents upon which pregnancy has little or no bearing, or finally; (3) if incidental are they influenced by the pregnancy ?

The subject of jaundice in pregnancy merits special investigation from this standpoint since there has been considerable confusion in obstetric literature about it. Recent investigations, both clinical and experimental, in hepatic disease have thrown some light on what has been a controversial question. The revival of liver biopsy has helped in its classification. The

work of Roholm and Iversen (1939), Dible, McMichael and Sherlock (1943), Brass and Axenfeld (1942), has shown that the different forms of icterus designated as "catarrhal jaundice", "homologous serum jaundice", "epidemic icterus", "post-arsenotherapy-jaundice" present similar pathological findings, namely, those of acute hepatitis. Liver biopsies have revealed pathological changes unknown to pathologists since such changes have been shown to be reversible and to disappear *pari passu* with clinical improvement. Gillman and Gillman (1945) have demonstrated in pellagra and other nutritional diseases a peculiar condition in the liver in which there is extensive accumulation of fat which disappears under treatment. The experimental work of Himsworth and Glynn (1944a, b) has opened up a new field in the pathology of liver disease.

The aetiology of liver damage in pregnancy as revealed by the symptoms of jaundice is still debatable. In pregnancy there may be repeated attacks of jaundice and this may appear early or late. The pregnant woman is more prone to acute liver atrophy than the non-pregnant. During the year 1932 (Peller, 1936) there was an incidence in England and Wales of 4.3 fatal cases of acute yellow atrophy in 100,000 pregnant women compared with 0.15 fatal cases in a similar number of non-pregnant.

The results of a clinico-pathological study are presented in this paper in the hope that they may elucidate the problem of icterus in pregnancy.

MATERIAL.

The cases are divided into 2 groups: (1) non-icteric (9 cases), and (2) icteric (12 cases). In all but one, liver biopsies were taken.

Group 1 included women whose preg-nancies were normal and others who had had renal disease, anaemia, hyperemesis gravidarum, malaria.

Seven of Group 2 (icteric) gave a short history common to infective hepatitis, namely, lack of appetite, nausea and hypochondriac pain. Jaundice occurred in the last trimester or early puerperium. One case with only slight jaundice had a strongly positive Wassermann reaction. Jaundice was first noticed during the second trimester in 2 cases and in the first trimester in another 2.

Space does not allow of detailed pathological description and discussion of all the cases and so the relevant information has been presented in as concise a way as possible, namely, in the form of tables (I and II). However, 3 cases have been chosen for more detailed comment since they are particularly apposite to our theme. Table III summarizes the biochemical findings.

The 3 cases which are described in detail will be found in Table II.

CASE 16 (a, b, c).

Nullipara, aged 20. Shortly after marriage she had an abortion at 6 weeks. Two months later she became pregnant again. During first 8 weeks had slight vomiting. At 20th week vomiting and anorexia were more marked. Patient noticed darker colour of urine and lighter colour of stools. Jaundice appeared about the 24th week with weakness.

27th November, 1944. Admission to clinic at about 28th week; heavily jaundiced; liver edge 2 fingers below costal margin, painful; spleen palpable.

Hb., 70 per cent (Sahli); red-blood cells, 3,800,000; white-blood cells, 8,000.

Urine—albumin +, bilirubin + + +, urobilinogen 0.

Serum protein—5.85 / 2.70 / 3.15.

Serum bilirubin—18.2 / 7.5 / 10.7.

Urea—40 mg. per cent; cholesterine—116 mg. per cent.

Liver-biopsy—see histological report.

28th November. Diarrhoea. Jaundice increased.

30th November. Prothrombin time, 21 minutes. Galactose excretion, 3 g. after 4 hours.

2nd December. Prothrombin time, 17 minutes.

4th December. Prothrombin time, 14 minutes. Takata-Ara + + +.

6th December. Spontaneous delivery of premature foetus (1,600 g.) which lived 8 hours. Placenta very yellow.

Autopsy did not reveal anything of note.

Next day, urine—bilirubin + + +, serum bilirubin, 16.4/9.8/6.6, serum protein 5.6/2.6/3.0.

The puerperium was afebrile but jaundice continued. Fourteen days after delivery the jaundice was less, the liver smaller and edge palpable only one finger below costal margin. Hb., 60 per cent (Sahli).

3rd January, 1945. Serum protein, 5.4/2.4/3.0. Serum bilirubin, 10.1/6.4/4.7.

Takata-Ara, + +. Urine—bilirubin, 0; urobilinogen +.

7th January. *Second liver-biopsy* (4 weeks after delivery and about 6 weeks after first biopsy).

Although jaundice still present and liver palpable the patient insisted on going home.

Seen one month later. Liver still palpable but jaundice absent. Serum protein 6.3/3.4/2.9. Serum bilirubin 2.7/1.6/1.1.

8th March. General condition satisfactory. Serum protein 6.1/4.1/1.0. Serum bilirubin 1.9/0.9/1.0.

17th April. Liver still palpable. Serum protein 7.5/5.0/2.5. Serum bilirubin 1.45 (only indirect). Takata-Ara 0.

20th May. *Third liver-biopsy.* (5½ months after delivery).

Patient not seen again until visit to antenatal clinic on 22nd October, 1945, when pregnant 8 weeks. Hb., 55 per cent (Sahli). No jaundice. Serum protein 7.25/4.6/2.65. Serum bilirubin 1.3 (indirect).

Returned 31st January, 1946. Symptomless. Serum protein 6.75/3.75/3.0. Serum bilirubin 3.36/0.18/3.18. Hb., 45 per cent (Sahli).

Full haematological examination revealed hypochromic, macrocytic, anaemia. Patient refused admission. When seen at 28th week no improvement in blood picture. Serum protein 6.6/3.9/2.7. Serum bilirubin 1.4/0.1/1.3 The patient was then lost sight of.

Description of Liver Biopsies.

First liver-biopsy. (Fig. 1. 28th week of pregnancy, jaundice marked.)

The lobular pattern is hardly recognizable owing to the liver-cell columns being broken up. There are small areas where liver-cells have entirely disappeared. Blood sinusoids with reticular framework and endothelial cells replace them. The surviving liver-cells show various necrotic and autolytic changes but there is also evidence of cell-proliferation. Biliary pigment is seen in many cells. The portal fields have an increase of fibrocytes and leucocytes. The periphery of some lobules is collapsed. The sinusoids are filled with much blood and show a distinct but not marked inflammatory infiltration.

Diagnosis. Severe acute and diffuse hepatitis.

Second liver-biopsy. (Fig. 2. Six weeks after the first biopsy and 4 weeks after delivery.)

The histological picture has entirely changed. The lobular pattern is now normal. The liver-cells are regular, large and laden with glycogen. The protoplasm appears light and the cell borders are clearly visible. The nuclei are rather big and generally vesicular. In a few liver-cells biliary pigment is visible. The portal fields are still marked but infiltration is much less striking than in the previous biopsy. Only fibrocytes can be found. Some portal fields are connected with each other by small lines of tissue rich in fibrocytes. The sinusoids are narrow. Kupffer cells are increased but they do not contain biliary pigment. There are only very few inflammatory cells to be seen.

Diagnosis. The liver has entirely recovered its structure. There is residual portal infiltration and an increase in reticulo-endothelial cells.

Third liver-biopsy. (Fig. 3. Five and a half months after delivery.)

The normal pattern is similar to that seen in the second biopsy. The portal fields are almost normal. There is no increase in fibrocytes but from some portal fields a few fibrils protrude into adjacent lobules. Kupffer cells are recognizable with difficulty. Sinusoids are narrow. Occasionally a liver cell containing bile pigment is seen.

Diagnosis. Normal liver.

CASE 20 (see Table II).

26th November, 1945. Primipara, aged 35. Seen in antenatal clinic, 36 weeks pregnant with pre-eclampsia (urine, 3 g., albumin; blood-pressure, 150/85; oedema of legs). Admitted to hospital.

8th December. Blood-pressure, 130/90. No albuminuria. Spontaneous twin delivery (1st breech, 2,550 g.; 2nd, vertex, 2,050 g.); Postpartum haemorrhage. Four days after delivery developed slight icterus; liver edge one finger below costal margin. Blood-pressure, 130/90. Albumin nil. Bilirubin +. Serum protein 5.3/2.5/2.8. Serum bilirubin 3.4/1.9/1.4. Blood urea 22 mg. per cent.

Liver-biopsy.

The next day, increase of icterus.

13th December. Blood-pressure, 175/110. Marked oedema both legs. During first 12 hours had 3 convulsions. Oedema increased but size of liver diminished. Icterus deeper. Urine, albumin +, bilirubin + +. Serum protein 5.3/2.2/3.1. At night the temperature rose to 38.8°C. and pulse to 140.

Next day, coma and death.

Autopsy. Dark green, very small (860 g.) liver. Consistency normal. Macroscopically no haemorrhage in the parenchyma, but small lighter stained areas evenly distributed. Kidneys icteric and swollen. Marked oedema of lungs and brain.

Histological Report of Liver Biopsy.

The liver-cell columns are intact and there is no necrosis. They are generally large and divided into sectors containing 2 different kinds of cells: (1) large polygonal cells rich in glycogen. Their nuclei are regular and mainly vesicular. (2)

Large irregularly-shaped cells with small nuclei and protoplasm very light and full of small vacuoles. There is very little glycogen in these cells. The sinusoids are large and the Kupffer cells greatly increased and containing much bile pigment. In places there are small accumulations of fibrocytes and round cells. The portal fields appear normal.

Diagnosis. Structurally the liver is unchanged except for extreme fatty degeneration. Hepatitis is not present.

Histological Report of Liver from Autopsy.

Several sections of the liver show the typical picture of extensive central fatty degeneration. There is heavy icterus particularly marked in the reticulo-endothelial cells. There is not any necrosis and very little inflammatory infiltration.

Changes which could be related to the existing eclampsia were not found either in the liver or kidneys.

Diagnosis. Icteric liver with extensive fatty degeneration (functional breakdown).

CASE 21 (not included in Table because liver-biopsy was not performed).

2-para, aged 24; one self-induced abortion. Until 16th week of this 4th pregnancy the patient was well. She then complained of fatigue, insomnia, and anorexia. Jaundice and darker urine now noticed. Patient was examined by physician who found liver edge palpable. Blood-pressure, 105/60; Hb., 65 per cent (Sahli). Red-blood cells, 3,100,000; white-blood cells, 4,700. Heyman's van den Bergh direct +, indirect +. Total bilirubin, 9.7 per cent. Takata-Ara o.

10th April, 1945. Admitted to obstetric clinic. Fundus at 20 weeks. Liver edge one finger below costal margin. Jaundice.

Urine albumin +, bilirubin + + +, urobilinogen +, urobilin +.

Serum bilirubin 5.07/3.51/1.56. Serum protein 6.9/2.4/4.5. Takata-Ara o.

For the next few days there was no change. A liver biopsy was not done because of a prothrombin time of 26 minutes (Quick's method). During

the next week the patient complained of constant pain in the liver region and jaundice deepened

20th April. General deterioration. Serum bilirubin 9.12/7.34/1.78. Prothrombin time 18 minutes. Interruption of pregnancy decided upon. The following day a vaginal hysterotomy was done under spinal anaesthesia.

2nd May. Postoperative course normal. Icterus almost disappeared. Urine normal. Serum protein 6.9/3.6/3.3.

TECHNIQUE OF HISTOLOGICAL PREPARATION OF LIVER BIOPSIES.

It is felt that a short description of the technique of histological preparation of liver-biopsies is not out of place. By fixing the fresh material in 10 per cent formalin and embedding in paraffin after methyl-benzoate-paraffin preparation a significant difference will be found in the general appearance of living as distinct from autopsy material. This has not been appreciated by previous workers who have always used absolute alcohol as a routine fixative, a procedure recently stressed by Sherlock (1945). Only a very small portion of the biopsy is fixed in alcohol in order to show the presence of glycogen. For the main histological examination alcohol is avoided owing to its shrinking effect. This influences the appearance of the cytoplasm and the shape of the sinusoid endothelium. In contradistinction to the general aspect of the cells in an autopsy liver those seen in a liver *in vivo* are larger, more polygonal with borders clearly visible and protoplasm light and only slightly eosinophilic. The vesicular nuclei, whose nuclear bodies are distinct, are relatively small compared with the amount of the cytoplasm. These cells are full of glycogen. However, when these cells correspond more to those in postmortem livers, namely, indistinct cell borders, dense protoplasm, more compact dark nuclei, then it has been found that the glycogen content

is less or even absent. This phenomenon is probably due to the close relationship between glycogen and water in the cells (Fenn, 1939).

COMMENT ON THE GROUP OF NON-ICTERIC CASES.

In this group the general appearance of the biopsy was that of a more or less "normal" liver. In some instances there were pathological changes which were the obvious result of a past or present illness. They were quite unrelated to pregnancy. Except in Case 3 where there was more infiltration, the portal fields appeared normal. In Cases 1 to 4 the increase in Kupffer cells and infiltration may be due to previous malaria since these changes have been noted repeatedly in cases of malaria and syphilis (Egeli and Laqueur, 1947).

Nearly all specimens showed a common variability in shape of cell and appearance of cytoplasm as well as varying degrees of cell-polymorphism. This last phenomenon can only be roughly estimated by simple inspection. But its real existence has been confirmed through cell and nuclear measurements by Eser, Eser and Ladewig (1944–45) of this University. Some of the biopsy material from this group of pregnant women have been examined by them. Much more marked cell variability than in the non-pregnant was found. Glycogen-content can only be estimated very crudely by morphological examination. It was interesting to note in Cases 5 and 9 that even by this rough measurement the glycogen was decreased. The former was a case of malnutrition and the latter hyperemesis gravidarum. It does not necessarily follow that in hyperemesis there is always depletion of glycogen in the liver cell. Case 8 is an exception, for this was a case of severe vomiting in pregnancy and
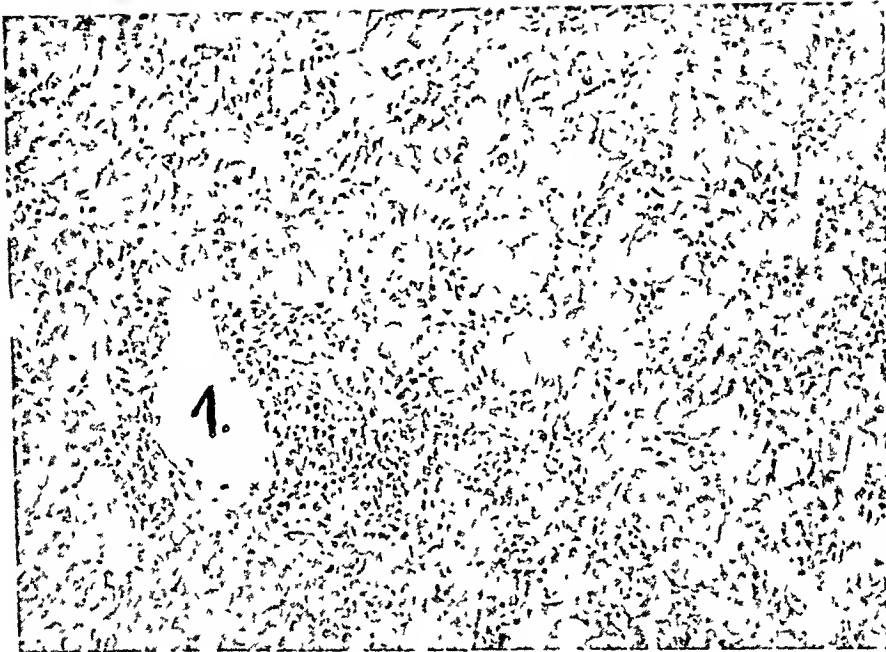
FIG 1

CASE 16a. Severe infective hepatitis, first liver biopsy, formol fixation, paraffin section, 7μ, H and E Photomicrograph $\times 250$
Marked changes in liver Cell columns broken up Liver cells showing various signs of necrobiosis and autolysis.
1 Sublobular vein surrounded by inflammatory cells Diffuse inflammation

W C W N
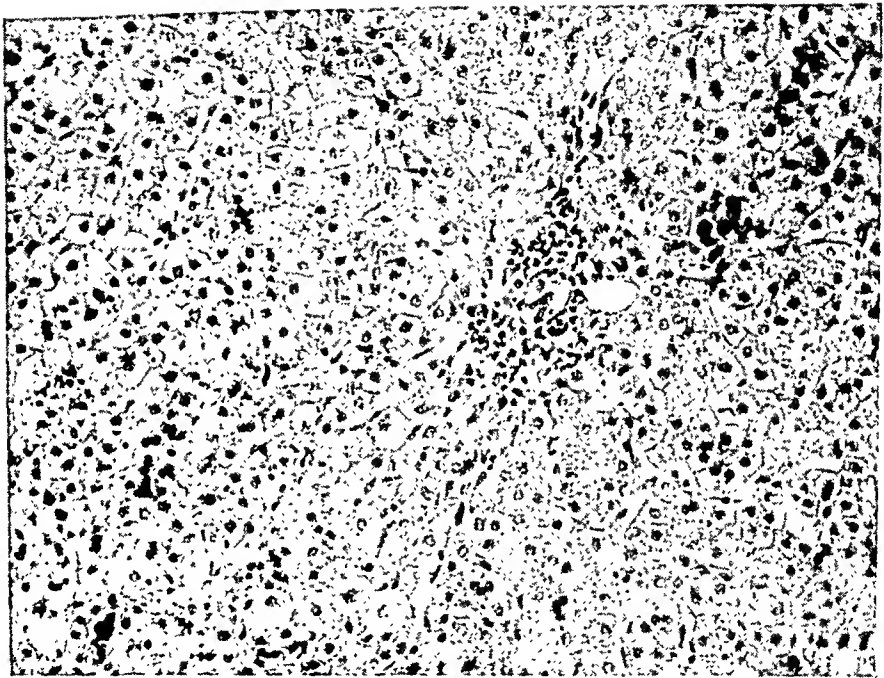
FIG. 2.

CASE 16b. Second liver biopsy, 6 weeks later, formol fixation, paraffin section, 7μ. Photomicrograph × 250.

Lobular pattern quite normal. Liver cells everywhere distinct, polygonal, borders sharp. Infiltration somewhat increased around portal field (1). At (2) biliary casts.

Liver structurally recovered after heavy hepatitis

W.C.W.N.
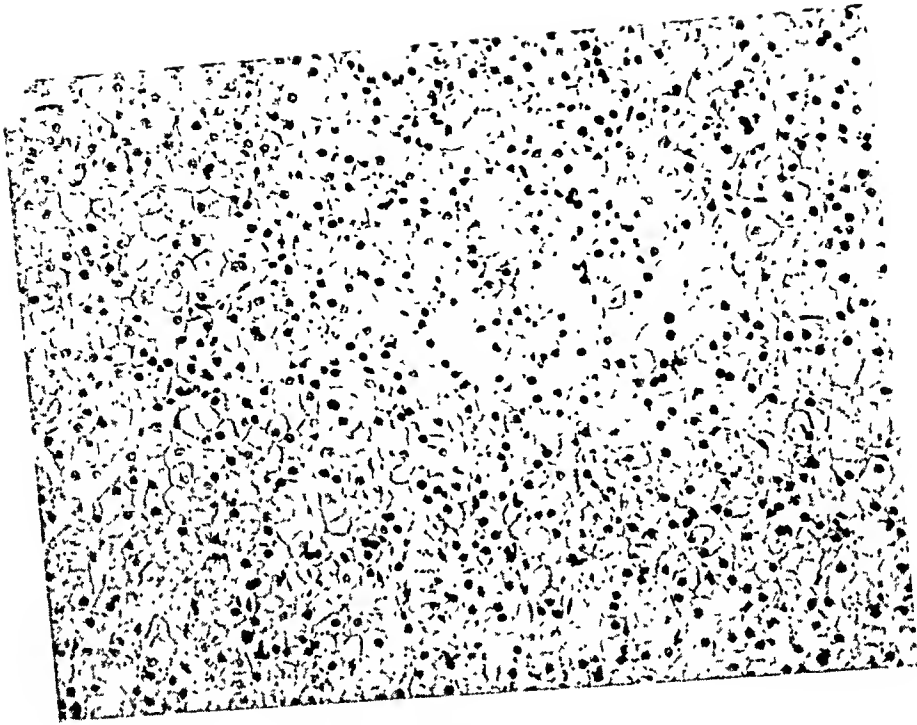
FIG. 3.

CASE 16c. Third liver biopsy, 5 months later. Formol fixation, paraffin
section, 7μ, H. and E. Photomicrograph × 250.
Normal liver pattern. Characteristic for specimens *in vivo*.

W.C.W.N.
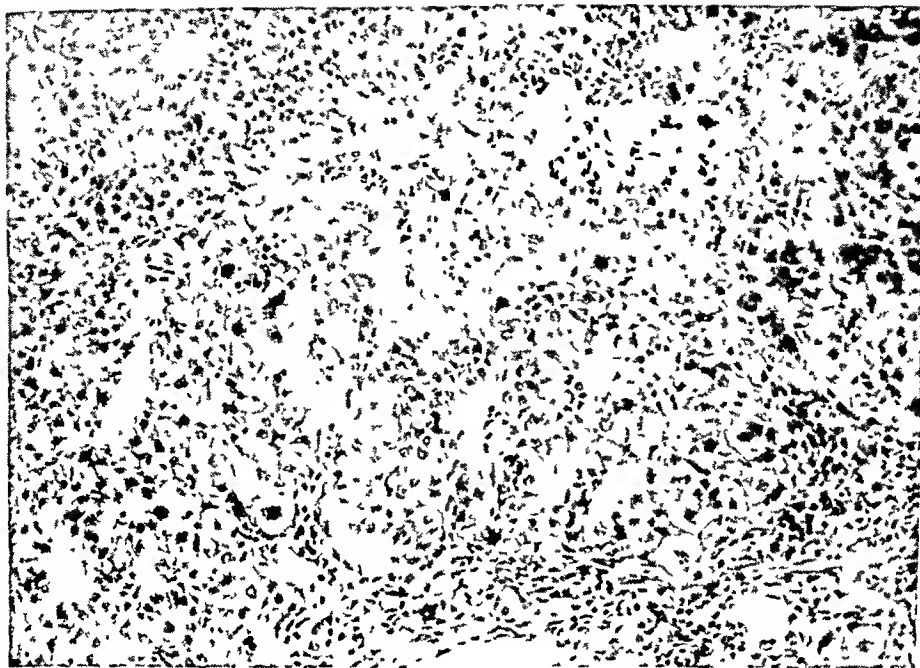
FIG 4

CÁSE 18a   Infective hepatitis   First liver biopsy, formol fixation, paraffin
section 7μ, H and E   Photomicrograph x 250
Severe destruction of liver with cell necrosis and inflammatory infiltration.
No increase in fibrous tissue   Pregnancy undisturbed

W C W N

the liver glycogen appeared more or less normal.

Of particular interest is Case 7 since the picture of the liver was normal despite severe renal disease.

Liver-biopsies taken from 9 pregnant women (non-icteric) have not revealed gross, uniform, morphological changes from which one would be enabled to make the diagnosis of "liver of pregnancy." (Hofbauer, 1928). In the past German obstetricians have belaboured this term unjustifiably. They have created such an entity based solely on functional findings which are notoriously unreliable. All that can be suggested is that there is a certain variability in cell-pattern about the liver in normal pregnancy, the significance of which cannot as yet be fully assessed. It may possibly be explained as being a morphological stigma of the strain of pregnancy. An extensive study of liver biopsies in non-pregnant and pregnant women (normal and toxaemic) has been described by Ingerslev and Teilum (1945) working in Copenhagen. Their findings are in agreement with ours in that the minor changes occurring in the liver during normal pregnancy are not specific enough to warrant the use of the term "liver of pregnancy" as though this were a histological entity.

COMMENT ON THE GROUP OF ICTERIC CASES

Nine cases of this group showed histological changes common to the various types of hepatitis. The findings did not differ in any respect from those described by previous investigators. In our material the diffuse acute form of hepatitis has prevailed. There were 2 patients in whom biopsies were repeated and in whom the liver showed complete restitution to normal without scarring. One case (9a) showed a striking appearance with casts in biliary capillaries, and these were also seen in Case 14 (Fig. 6) after 5 weeks of jaundice. Others have described such an occlusion-component which can be found frequently at the end of an attack of jaundice.

Case 7 is of interest because of the severity of the initial hepatic lesions and the complete recovery of the liver. The first liver-biopsy raised the question as to whether the case was one of acute atrophy of the liver. However, in view of the entire lack of connective-tissue reaction—the parenchyma-free spaces consisted only of collapsed reticulum—it was decided to diagnose the case as one of very severe hepatitis. With the slow clinical recovery a subchronic type with scarring was anticipated but the second biopsy proved this conjecture to be wrong. It showed the process to be already arrested and the liver on the way to recovery. The connective-tissue fibres around the portal fields were so slender and fine that the term "scarring" was hardly applicable. Finally, the third biopsy (Fig. 3) revealed a normal liver-pattern. Clinical improvement as assessed by biochemical results (see Table III) did not keep in step with the histological progress. The albumin-globulin quotient of the serum protein returned quickly to normal but total protein was slow in this respect. The bile pigments in the blood never reached normal and the presence of bilirubin (indirect Heymans van den Bergh) was striking. We are not able to explain this.

Case 8 was typical of fulminating acute yellow atrophy. It was difficult to decide whether or not massive necrosis was superimposed upon hepatitis. The patient was seen 3 weeks before jaundice developed. When she was admitted jaundice had been present for only 3 days. Her nutritional state was poor and the serum protein low but not under 5 per cent.

Case 10 had two biopsies which did not

show changes due to hepatitis although there had been a history of icterus. The main histological features were a normal general structure of the liver with unaffected portal fields, a certain irregularity in shape of the liver-cells and their nuclei and a deficiency of glycogen. Although there were not marked changes in the histological pattern of the second biopsy yet clinically the patient had deteriorated and the serum protein showed an inversion of the albumin/globulin quotient. Cell polymorphism and reticulo-endothelial reaction were more marked and bile pigment had increased. It was unfortunate that this patient did not return for further investigations.

Case 21, to which reference has already been made and on which a biopsy was not performed, was clinically almost identical with the above. In spite of treatment her condition became worse and there was an inversion of the serum-protein. After interruption of pregnancy there was a quick and full recovery.

Case 20 is difficult to interpret. Pre-eclampsia and postpartum convulsions confused the issue. It is not usual to find icterus with a true eclampsia. The clinical course suggested acute liver atrophy since the liver became significantly smaller and the jaundice more intense. The albumin/globulin quotient below 1 might have been due to the pre-eclampsia and its further fall within 24 hours was in favour of severe liver damage. The liver-biopsy as well as the postmortem liver revealed changes which could not be explained except by some kind of acute intoxication resulting in fatty degeneration. Such changes are seen in acute phosphorus poisoning. It is possible that this case was one of sudden functional breakdown of the liver owing to the strain of this particular pregnancy. Rabau (1929) has described such catastrophies in pregnancy. It is suggested that

this case and the 2 preceding belong to the same clinical and pathological group.

On the basis of the pathological findings already discussed the clinical material (icteric and non-icteric cases) can be divided into 3 groups. The biochemical findings (Table III) support such a division:

(1) Non-jaundiced cases with more or less "hepatic strain".

(2) Jaundiced cases with histological findings similar to group (1).

(3) Jaundiced cases with a histological picture corresponding to hepatitis with a subgroup verging into acute liver atrophy.

DISCUSSION.

From our observations it would appear that jaundice may develop in pregnancy *per se* (icterus of pregnancy). On the other hand this symptom may be quite fortuitous, unrelated to pregnancy and due to infective hepatitis (concomitant icterus). Examination of liver-biopsies supports this differentiation. In pregnancy the liver may show functional peculiarities of its main metabolic processes which in themselves need not be considered pathological. Routine biopsies from pregnant women give the impression of normal liver structure to which sometimes are added minor histological deviations such as the difference in shape of liver-cells with increase in number of large nuclei, irregularities of the nuclei, increased glycogen load of the cytoplasm. All these are an expression of the lability of the liver and can be compared with the marked variations of liver-function tests in normal pregnancy. Pregnancy induces such changes which serve to demonstrate what might be termed "hepatic resilience".

Case 16 showed clinically a severe and progressive icterus, which had already manifested itself at the 10th week of gestation. There had been jaundice in a

	Protoplasm	Portal fields
ı-	Generally dense granular. Only at a few places spongy.	Within the mass of connective tissue difficult to differentiate. In some places increase of biliary capillaries
ɔact, ᴨts	Relatively dense with many small vacuoles. Spongy cytoplasm in places	A little more marked by cell infiltration
lar ele- yknotic ɔporadic nuclei	Generally light, sometimes more dense around the nuclei. Glycogen variable	Marked by cellular infiltration. No increase of connective tissue. Some accumulation of connective tissue within the lobule (collapse areas)
ar. Many Frequently	More or less light, spongy, and equally distributed in the cell body	Still infiltrated but inflammatory cells nearly disappeared, in some places tiny fibres intruding into lobules. Some increase of fibres in still affected areas
lar	Dense, strongly eosinophil. Very little glycogen	Not marked, no cell infiltration
ess regular and , many double ɩt forms	The same as in previous biopsy	The same as in previous biopsy
cular, very many ɔ, many double	In some parts light and heavily laden with glycogen, in others dense and nearly glycogen free, many vacuoles in central parts of the lobules	No inflammatory infiltration

Fat	Reticulo-endothelial system	Pigment	Diagnosis
None	Heavy inflammatory infiltration. Reticulo-endothelial cells indistinguishable	?	Massive liver necrosis. Acute yellow atrophy
?	Some inflammatory infiltration. Increase in number of Kupffer cells. Sinusoids enlarged and often hyperaemic	Some capillary casts	Acute yellow atrophy with signs of regeneration
None	Kupffer cells a little increased in number and enlarged. Sinusoids full of inflammatory cells especially marked in the neighbourhood of necroses	Very little biliary pigment	Acute hepatitis. Heavy parenchymal damage. Central necroses
None	Kupffer cells normal. No inflammatory infiltration in the sinusoids	Very frequent biliary casts in capillaries	Liver in state of restitution, a little scarring
?	No pathological changes	Traces of biliary pigment, rare	Normal liver, poor in glycogen
?	Increase in number of Kupffer cells, these cells being often enlarged and swollen	Biliary pigment rather frequent in reticulum cells	Liver poor in gylcogen with marked reticulo-endothelial activity
+ + in central parts	Increase in Kupffer cells	Biliary pigment in liver cells and reticulum cells + +	Liver with heavy central fatty degeneration. Icterus

TABLE III

Results of Blood Analysis

Case	Time of examination	Serumbilirubin Total	Direct	Indirect	Serumprotein Total	Albumin	Globulin	A/G Quot.	Takata-Ara	Remarks
1	After 10 days jaundice	1.90	0.72	1.18	4.90	2.72	2.18	1.25	0	Non-icteric, anaemia
5	On admission	0.2	0.05	0.15	5.2	3.1	2.1	1.48	—	Non-icteric, malnutrition
8	On admission	0.31	0.19	0.12	5.10	3.0	2.1	1.43	—	Hyperemesis gravidarum
9	On admission	0.95	0.38	0.57	6.32	4.56	1.76	2.59	—	Hyperemesis gravidarum
10	2nd day of puerperium	16.4	9.12	7.78	—	—	—	—	++	Hepatitis (jaundice)
	14 days later	1.7	1.36	0.34	—	—	—	—	0	
11	2nd day of puerperium	12.7	7.3	5.4	—	—	—	—	++	Hepatitis (jaundice)
	10 days later	8.28	4.78	3.5	—	—	—	—	±	
12	On admission	13.7	8.5	5.2	—	—	—	—	+	Hepatitis (jaundice)
13	On admission	1.5	0.9	0.6	6.75	3.8	2.95	1.25	0	Jaundice
14	On admission	3.48	1.4	2.08	5.85	3.8	2.05	1.85	0	Hepatitis (4th week of icterus)
16	On admission	18.2	7.5	10.7	5.85	2.7	3.15	0.85	+++	Very heavy hepatitis
	10 days later	16.4	9.8	6.6	—	—	—	—	++	
	1 month later	10.10	6.4	4.7	5.4	3.0	2.4	1.25	+	2nd biopsy
	2 months later	2.70	1.6	1.1	6.3	3.4	2.9	1.21	0	
	3 months later	1.9	0.9	1.0	6.10	4.1	2.0	2.05	0	3rd biopsy
	6 months later	1.45	0.	1.45	—	—	—	—	0	Again pregnant
	10 months later	1.30	0.	1.30	7.25	4.6	2.65	1.74	0	
	14 months later	3.36	0.18	3.24	6.75	3.75	3.0	1.25	0	28th week
	15 months later	1.45	0.1	1.35	6.6	3.90	2.7	1.44	0	
18	On admission	14.7	10.7	4.0	5.4	3.3	2.1	1.75	+++	Hepatitis (jaundice)
	15 days later	3.93	2.34	1.59	6.50	4.1	2.4	1.71	0	2nd biopsy
17	On admission	14.6	9.6	5.0	5.0	2.85	2.15	1.35	—	Acute yellow atrophy
	3 days later	16.5	11.3	5.2	4.9	2.65	2.25	1.18	—	2nd biopsy, death
19	On admission	9.24	5.32	3.92	6.75	3.45	3.3	1.05	±	Pregnancy jaundice
	14 days later	10.5	6.84	3.66	5.85	2.1	3.75	0.57	±	
21	5th week of jaundice	5.07	3.51	1.56	6.80	3.2	3.6	0.89	0	Pregnancy jaundice—no biopsy
	10 days later	9.12	7.34	1.78	6.90	2.4	4.5	0.53	0	Vaginal hysterotomy
	14 days later	2.3	1.5	0.8	6.9	3.6	3.3	1.1	0	
20	5th day of puerperium	3.4	1.9	1.5	5.3	2.5	2.8	0.89	—	Pre-eclampsia, icterus, functional liver breakdown. Death
	2 days later	—	—	—	5.3	2.2	3.1	0.71	—	

previous pregnancy. Yet the histological pattern of the liver was not very different from that seen in an unjaundiced pregnant woman. A second biopsy a fortnight later revealed only a slight aggravation so far as bile pigment was concerned and parenchymal damage was absent. At the same time the total serum-protein had dropped significantly with the serum-albumin decreasing and the globulin increasing with resultant inversion of the quotient.

This inversion of the albumin/globulin quotient is an important finding particularly as it can occur without visible morphological hepatic damage. It serves to differentiate the various types of jaundice in pregnancy. In infective hepatitis the serum proteins are more or less normal and especially the albumin/globulin quotient (Maclagen, 1944; British Medical Journal, 1944; Teitelbaum, Curtis and Goldhammer, 1945). When in infective hepatitis there is inversion of this quotient it is a sign of the process becoming chronic and indicates scarring if such a liver were to be examined histologically. Higgins, O'Brien, Stewart and Witts (1944) have pointed out that the value of serum-protein estimation lies more in prognosis than diagnosis. In all our cases where hepatitis was diagnosed histologically there was an albumin/globulin ratio above 1 (the first estimation in case 16 was an exception). In 3 others there was an inverted ratio. Thus, in the absence of liver-biopsy, serum-protein estimations do help in distinguishing the type of jaundice. Liver-biopsy when properly performed does not carry a greater risk than certain other diagnostic procedures (Egeli, 1945). The work of Sherlock (1945) also confirms this. For those who are reluctant to perform liver-biopsy it is possible to differentiate between infective hepatitis or jaundice of pregnancy by noting the level of the serum-protein. Case 21 in which there was no liver-biopsy

is an instance where the recognized treatment (glucose, insulin, nicotinic acid, etc.) recommended by Beiglböck and Spiess-Bertschinger (1944) for parenchymal hepatic disorders failed to influence the intensity of the jaundice. However, when pregnancy was terminated there was a rapid return to normal health. Termination of pregnancy will continue to be the treatment in this type of " jaundice of pregnancy " until more is learnt about its aetiology. It is possible that the administration of protein dialysates may in the future ameliorate the condition. There was no opportunity to treat such a case with these substances for they were not available in Turkey at the time. In this case it was pregnancy that precipitated the jaundice and therefore it falls into the group " toxaemia of pregnancy " for want of a better term.

Infective hepatitis in pregnancy is in quite a different category. The main question here is whether or not the pregnancy is able to influence the course of the hepatitis. This disease has its specific aetiology quite unrelated to pregnancy. Termination of pregnancy should be considered only if the hepatitis is of such severity that the life of the expectant mother is in serious danger. Statistics already quoted and the examples of Himsworth and Glynn (1944a) do show that pregnancy can influence infective hepatitis adversely. Ballot (1859) has described an epidemic in which 8 pregnant women were attacked by hepatitis and 7 of them died shortly before delivery. Hardie (1889–90) reported a case of a young boy who had a mild attack of hepatitis. His pregnant sister later became jaundiced and died of acute yellow atrophy of the liver. Hayward (1889–90) has the bizarre record of a pregnant woman who died of acute yellow atrophy and 10 days later her husband developed infective hepatitis.
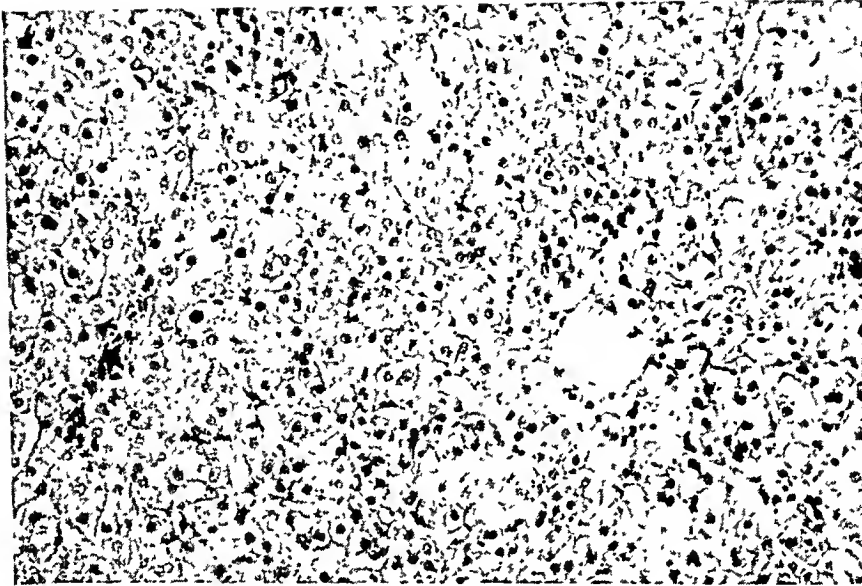
FIG. 5.

CASE 18b. Second biopsy a fortnight later. Formol fixation, paraffin section, 7μ, H. and E. Photomicrograph × 250.
Liver almost recovered. Minor structural irregularities and mesenchymal reaction   Pregnancy continued.

W.C.W.N.
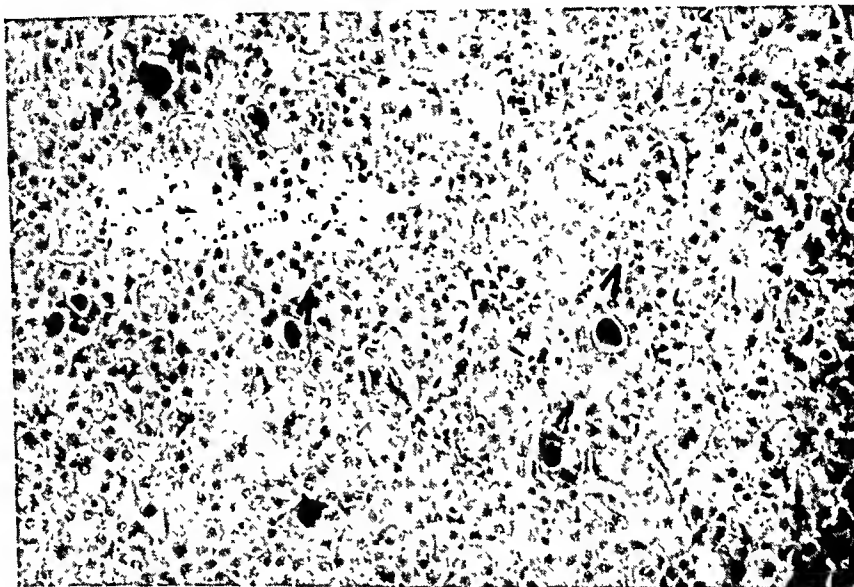
FIG. 6

CASE 14. Infective hepatitis fifth week. Liver biopsy, formol fixation, paraffin section 7μ, H. and E. Photomicrograph × 250.
Liver structure nearly normal but note numerous casts in biliary capillaries. (Occlusion component.) 1. Biliary casts.

W.C.W.N.

FIG. 7.

CASE 17a   Massive hepatic necrosis (acute yellow liver atrophy). Liver biopsy, formol fixation, paraffin section 7μ, H. and E. Photomicrograph × 250

Liver entirely destroyed. Third day of jaundice

Some surviving liver-cells within huge field of necrosis

1 Liver-cells.   2 Biliary capillaries   3 Portal vein.
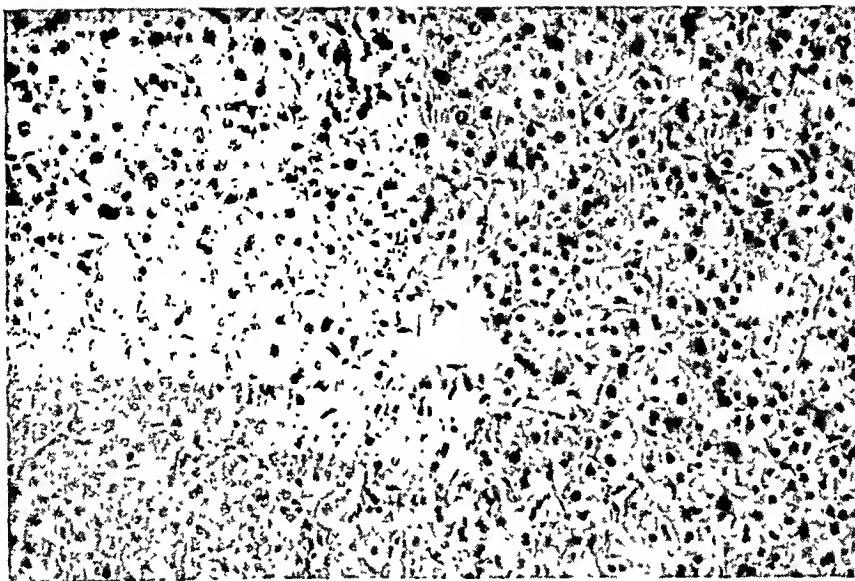
FIG. 8.

CASE 19. Pregnancy icterus. Liver biopsy, formol fixation, paraffin section, 7μ, H. and E. Photomicrograph × 250.
In spite of severe clinical condition, only slight changes in the liver. Liver-cell columns unbroken, no major cell alterations, no inflammatory infiltration.
Note the marked difference between this figure and figures 1 and 4.

W.C.W.N.

A common complication of acute infective hepatitis is the transition to a chronic form with development of cirrhosis. Massive necrosis is uncommon. But Himsworth and Glynn (1944a) have indicated that the extra strain of pregnancy superimposed on infective hepatitis may contribute to a disastrous massive necrosis. They have underlined the nutritional element, deficiency of protein especially methionin, as a causal factor. German authors (Seyfarth, 1921; Strumpell, 1921) have described how in the first world war the incidence of acute liver atrophy was greatly increased and was related to the general malnutrition of their people. The one patient in our series who succumbed to massive necrosis belonged to the lowest economic group. There was in 1936–37 in Istanbul (Liepmann, 1938) an epidemic of massive hepatic necrosis. The mortality was greatest among the poorest elements of the population.

We are unaware of any extensive experimental work having been done on this problem during pregnancy. Croft and Peters (1945) found that in rats the administration of methionin compensated for nitrogen loss after burns. Harrison and Long (1945) report that the restoration of depleted liver protein depends on sufficient protein (S-compounds) in the food. The importance of protein in the diet for the maintenance of hepatic cytoplasm has been emphasized by Kosterlitz (1945). When one recalls the large amount of nitrogen which a pregnant woman needs for the foetus and later for lactation one must agree with Himsworth and Glynn that nutrition may be a conditioning factor in the aetiology of certain diseases. Thus the prognosis of infective hepatitis complicating pregnancy will depend on the nutritional state. The better this is the less the risk of an infective hepatitis progressing to acute atrophy. The treatment of infective hepatitis in pregnancy should be directed towards the prevention of massive necrosis. It is controversial whether evacuation of the uterus will influence the final changes in the liver. It may prevent massive necrosis. Liepmann (1938) in contrast to many obstetricians, was of the opinion that acute liver atrophy should not be included in the toxaemias of pregnancy. We are of the same opinion and suggest that termination of pregnancy should not be the invariable rule. Such intervention rids the mother of the foetus but it does not treat the infective hepatitis. Treatment should be guided by the nutritional state. If in the early stages of jaundice malnutrition is obvious then termination must be seriously considered. On the other hand, if the level of nutrition is high then interruption of pregnancy is not such an urgent necessity. The fate of the foetus is always doubtful in severe jaundice. Kehrer has shown that cholic acid and its derivatives may stimulate the uterus into activity.

CONCLUSION.

(1) Cases of icterus in pregnancy have been investigated and the findings of liver-biopsies described.

(2) Examination of liver-biopsy material reveals two types of jaundice, the one aetiologically related to the state of pregnancy without striking histological changes (jaundice of pregnancy), the other representing the condition of infective hepatitis (concomitant jaundice).

(3) In the absence of liver-biopsy, serum-protein estimation is a valuable aid. When in jaundice of short duration an inversion of the albumin/globulin ratio is found, then "jaundice of pregnancy" is to be suspected.

(4) Whether infective jaundice will proceed to acute yellow atrophy depends on the nutrition of the mother.

(5) " Jaundice of pregnancy " should be treated by termination of the pregnancy. In "concomitant jaundice" (infective hepatitis) a poor nutritional state- and severe course of the illness call for an interruption of the pregnancy. Otherwise the hepatitis should be treated by general medical measures.

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Gestational Changes in the Vaginal Epithelium and Their Relation to the Sex of the Foetus

BY

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THE value of the vaginal smear in the study of normal changes of the epithelium during the menstrual cycle has been extensively described (De Allende, Shorr and Hartman, 1943; Benedek and Rubinstein, 1942). Its abnormal changes in endocrine disorders and ready response to exogenous hormones has been demonstrated (Rubinstein, 1940; Shorr, 1945; Papanicolaou and Shorr, 1936; Greenblatt, Torpin and Brown, 1940; Greenblatt, 1940).

Relatively little is known about changes in the vaginal smear during pregnancy. The object of this study was to discover the normal changes in the vaginal epithelium during various stages of pregnancy and any possible relation of abnormal changes to the pathology of pregnancy.

MATERIAL AND METHOD.

Routine vaginal smears were taken in the antenatal clinic of the British Postgraduate Medical School. A total of 280 smears from 253 pregnant women were examined. The smears were taken during the 8th and 36th weeks of pregnancy. An ordinary cotton applicator was inserted into the vagina as far as between the midvagina and posterior fornix. It was twirled around a few times and then rolled upon a clean slide. The smear was then fixed immediately in a solution of equal parts of 95 per cent alcohol and ether.

After fixation for at least 10 minutes the slides were stained by the following method.

(1) Ehrlich's haematoxylin, 5 to 10 minutes (depending on the age of the staining solution).

(2) Dipped into water quickly 3 or 4 times.

(3) Best's carmine, 10 to 15 minutes.

(4) Best's differentiator for 3 seconds.

(5) Absolute alcohol, 2 immersions.

(6) Xylol.

(7) Mount with balsam.

The cytoplasm stains blue or deep red, depending on the presence of glycogen in the cells. In some cells the glycogen appears in deep red, coarse granules, while in others they are so fine that their cytoplasm is diffusely pink. The nuclei stain blue.

RESULTS.

During pregnancy an increasing hypertrophy of the vaginal epithelium takes place and causes a crowding of the epithelial cells, which acquire peculiar and characteristic forms. These cells were first described by Papanicolaou (1925) as navicular, oyster-shell, round or oval forms. The main characteristic of the vaginal epithelium during pregnancy is the increas-

ingly massive desquamation of cells. They are very rich in glycogen, and mostly contain round or oval-shaped, vesicular or, in the late stages, rod-shaped, pyknotic nuclei. A large number of such nuclei are freely scattered in large aggregations of cells.

The increase in the number of cells is accompanied by a progressive decrease in size and an increase in glycogen content. The nuclei are at first large, round and vesicular and tend to become oval-shaped (Fig. 1). With advancing pregnancy the appearance of medium-size cells with large round or oval vesicular nuclei can be noted. The cytoplasm shows increasing amounts of glycogen.

Before and about the 20th week cells characteristic of the later stage of pregnancy are present. They are smaller in size with rod-shaped pyknotic nuclei and are very rich in glycogen. They usually also occur during the luteal phase in small numbers and the term "luteal cells" is suggested for this type. Between approximately the 20th and 30th week increasing numbers of luteal cells appear, while the number of cells representing the earlier stages of pregnancy decreases.

After approximately the 30th week, luteal cells are either found exclusively or in combination with varying amounts of mucoid cells (Fig. 2).

These changes in the vaginal mucosa during the whole period of pregnancy may be associated with the appearance of mucoid cells, leucocytes and bacteria. The number of mucoid cells present in the vaginal smear has no relation to the stage of pregnancy.

In addition to smears showing the typical progressive changes of pregnancy 53 women, or 20.9 per cent, showed 3 specific atypical types of smear and a 4th type consisting entirely of polymorphonuclears.

I. *Mucoid-Cornified Smear*.

From about the 10th to the 17th week, approximately 50 per cent of the smears consisted of a large amount of mucous and mucoid cells with varying amounts of scattered, large, cornified cells with small, round, pyknotic nuclei (Fig. 3). This type of smear tended to disappear after about the 26th week and occurred only rarely up to the 30th week. It was, however, frequently encountered in patients with amenorrhoea, early menopause and fibromyomata. A total of 23 women presented this type of smear and 19 of these, or 82.6 per cent, were delivered of male infants.

II. *Cytolytic Smear*.

This was characterized by marked disintegration of cells, scattered nuclei and fragments of cytoplasm (Figs. 4 and 5). In addition a large number of Döderlein bacilli were present (Fig. 5). An equal number of Döderlein bacilli were present in other smears which showed no, or only little, cytolysis. This smear occurred mainly between the 25th and 36th week of pregnancy and was rarely seen before the 15th to 17th week.

Eighteen of 22 women (87.8 per cent) who showed this type of smear were delivered of female infants. Such of these smears as were taken exclusively between the 25th to 36th week of pregnancy corresponded in every case to the female foetal sex.

III. *Glycolytic Smear*.

The striking characteristic of this smear was the extracellular location of glycogen associated with intracellular glycopenia This type of smear is very infrequent and it was found in only 8 women. It was thought that loss of glycogen from the cytoplasm was caused by faulty technique in staining. Careful revision of the technique and repeated staining

revealed this type to be a specific type of smear. It occurred between the 18th and 36th week of pregnancy. All 8 women were delivered of male infants.

IV. *Leucocytic Smear*.

This consisted of polymorphonuclear leucocytes only and was found frequently during all stages of pregnancy.

Specific Smears of Late Pregnancy.

In late pregnancy the predominance of mucoid cells may be regarded as an androgenic feature and probably associated with a male foetus, while its absence in a markedly oestrogenic smear of late pregnancy points to a female foetus. Twenty-one of the 24 women, or 87.5 per cent, who presented between the 30th and 35th week a smear consisting almost entirely of small, glycogen-containing cells with rod-shaped, pyknotic nuclei (Fig. 2), were delivered of female infants. The presence of additional, increased amounts of mucoid cells occurred during the stage of pregnancy in 18 women. In 16 cases, or 88.9 per cent, a male infant was delivered.

DISCUSSION.

Investigation failed to reveal any evidence that these atypical specific smears are to be regarded as an accompanying or a prodromal feature of toxaemia or threatened abortion. Cornification, cytolysis, cellular glycopenia or increased deposition of glycogen and, in fact, in one case, an atrophic smear consisting entirely of basal cells, were of no significance as to the course of pregnancy. •

No correlation to the foetal sex could be established with the typical nonspecific smears during early and advanced pregnancy.

The correlation of specific changes in the vaginal epithelium with foetal sex is in keeping with the data presented by Burrows, MacLeod and Warren (1942) on the variation of excretion of 17-Ketosteroid during pregnancy in accordance with the sex of the foetus. The recent reports on determination of foetal sex by the injection of maternal serum into the immature mouse (Zavadovsky, *et al.*, 1943) or maternal urine or serum into the rabbit (Geisendorf, 1946) throw further light on this question. Extensive studies on the response of the human and animal vaginal epithelium to endogenous and exogenous hormones have revealed that oestrogens produce cornification and deposition of glycogen (Shorr, 1945; Papanicolaou and Shaw, 1936; Greenblatt, Torpin, Brown, 1940; Greenblatt, 1940; Rakoff, Feo and Goldstein, 1944) while progestogens cause increased desquamation of cells and thus inhibit cornification (Rubinstein, 1940). Progestogens do not inhibit deposition of glycogen unless present in large amounts, when they produce extensive cytolysis with glycopenia (De Allende, Shorr and Hartman, 1943). Androgens produce increased mucification of the vaginal epithelium (Nelson and Gallagher, 1936; Korenchevsky and Hall, 1937; MacDonald and Robson, 1939) and, unless in abnormally great strength, they do not inhibit cornification in presence of oestrogens. In fact their antagonism at slightly raised levels seems to be directed against the luteal hormone rather than the oestrogens, since they inhibit desquamation and thus permit the cells to cornify under the action of oestrogens. This is the most likely explanation of the mucoid-cornified type of smear which may occur during pregnancy and other conditions when a shift in the androgen-oestrogen ratio occurs toward an absolute or relative increase in androgens.

Since androgens, gonadotrophins and oestrogens in the maternal blood may vary with the foetal sex, the vaginal epithe-

lium is subject to the same changes. The intensity of hormonal activity and vaginal response determine whether or not a specific type of smear is produced. The results obtained show the wide range of normal variation in the vaginal smear during the gestational period and the difficulty of using this as a diagnostic method for abnormal changes in hormonal levels during pregnancy.

This method is not recommended for prenatal determination of sex, although in certain cases a correlation to the foetal sex exists. In this study 95 among 253, or only 37.5 per cent of pregnant women, showed such changes in the vaginal epithelium as could be interpreted as being due to the influence of the foetal sex. Even in the presence of the definite, specific types of smear an error of 11.9 per cent occurred.

SUMMARY.

A total of 280 smears was taken from 253 pregnant women during the 8th to 36th week of pregnancy. In addition to the progressive changes in the vaginal epithelium with advancing pregnancy, 3 specific types of smears were observed. These are the mucoid-cornified, the cytolytic and glycolytic smears. The absence of any relation to pathological changes during pregnancy was established and their correlation to the foetal sex indicated.

I wish to thank Professor James Young for his encouragement and guidance in carrying out this investigation. Thanks are due to Mr. John Baker of the Department of Pathology, who advised on the staining procedures.

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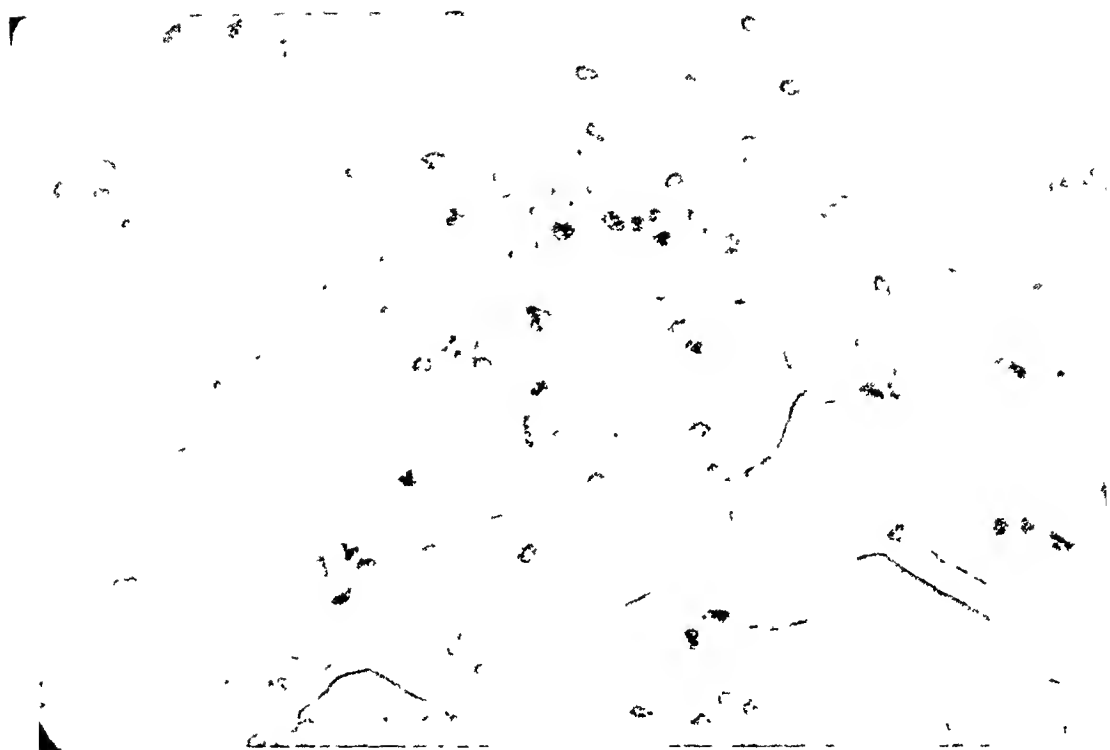
FIG 1 Vaginal Smear Twelve weeks' pregnancy (High power)
(Note large size of cells with large round and oval vesicular nuclei Single cornified and luteal cells)

J C N.
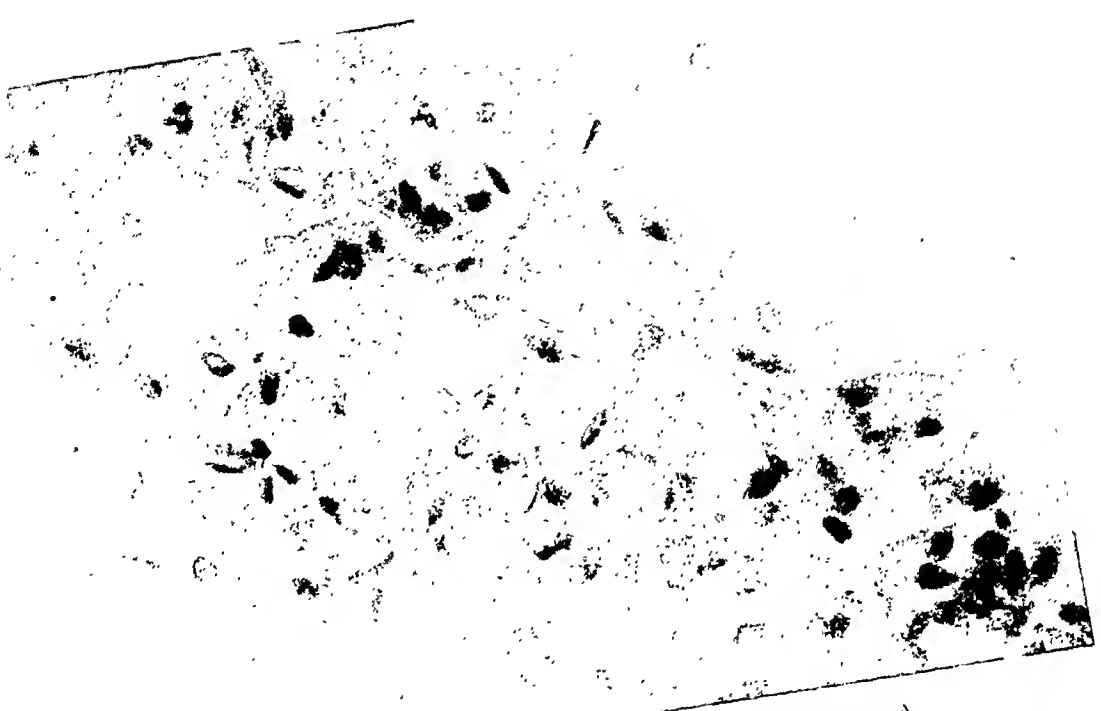
FIG. 2. Vaginal Smear. Thirty-six weeks' pregnancy (High power). (Note aggregations of small cells rich in glycogen with rod-shaped pyknotic nuclei. This woman was delivered of a female infant.)

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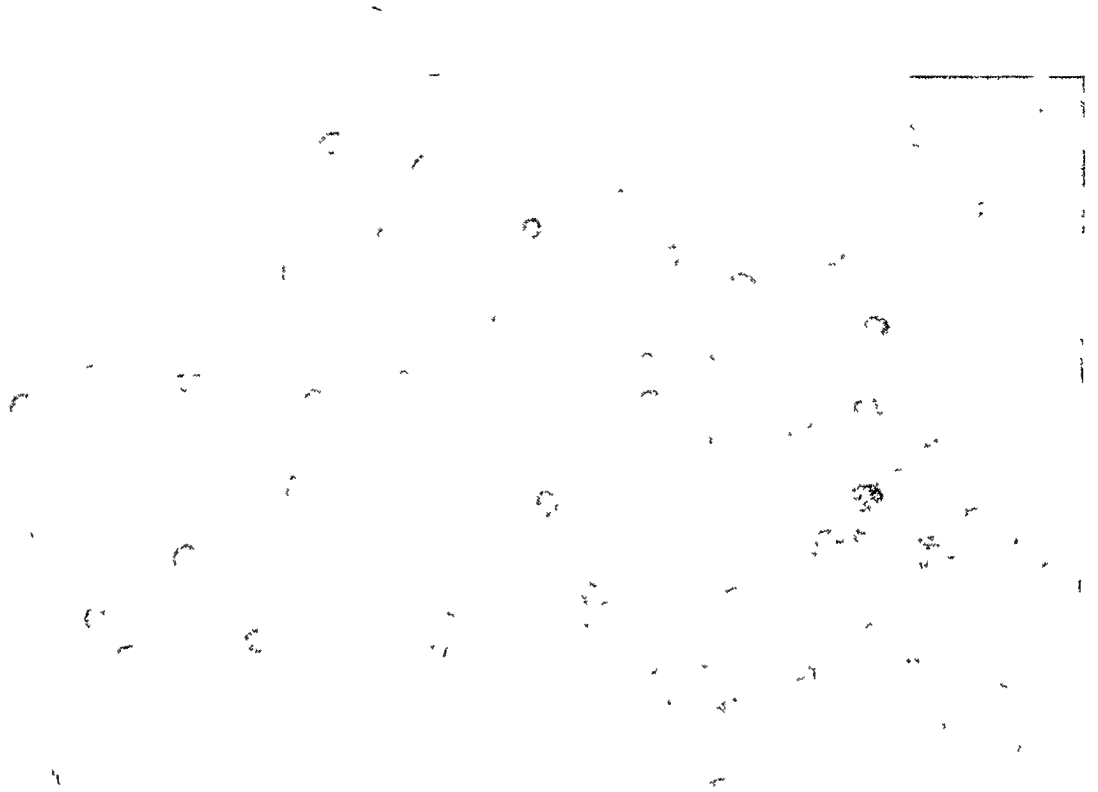
Fig. 3 Mucoid-cornified smear. Nineteen weeks' pregnancy (High power). (Note predominantly cornified cells and the hazy appearance due to abundant mucoid material. This woman was delivered of a male infant.)

H.E.N.
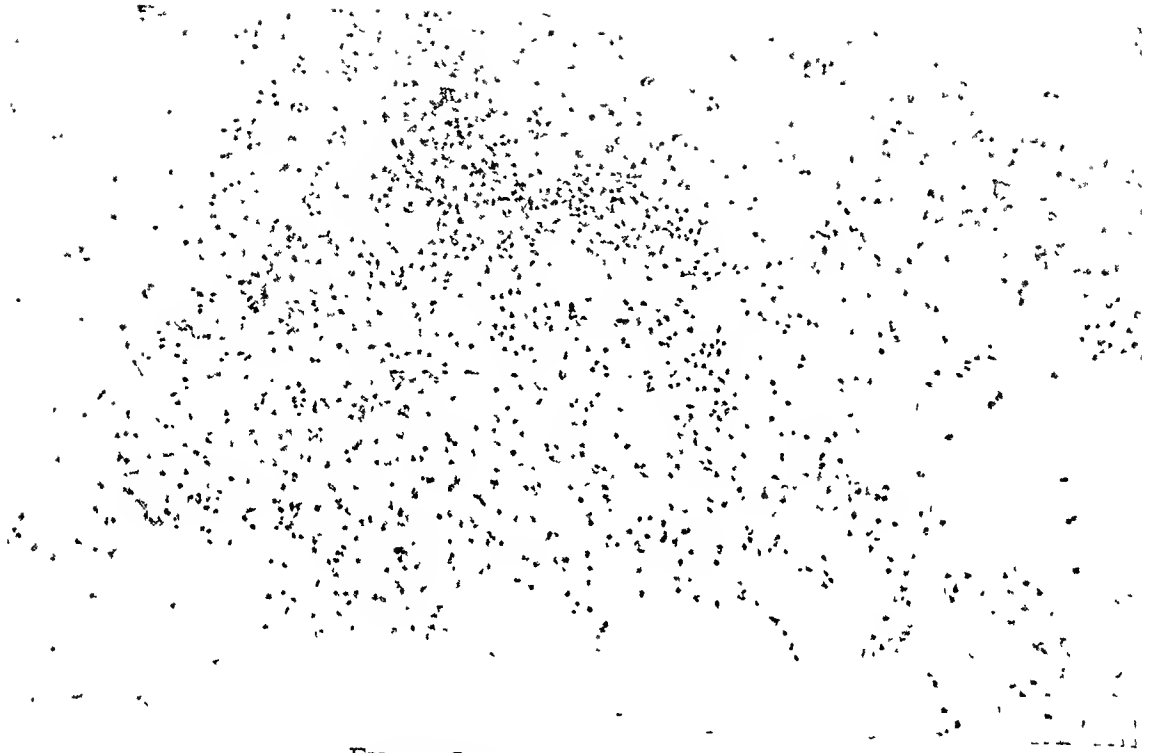
FIG. 4. Cytolytic smear (Low power).
(Note complete destruction of cellular cytoplasm without affecting the nuclei.)

H.E.N.

FIG. 3. Mucoid-cornified smear. Nineteen weeks' pregnancy (High power). (Note predominantly cornified cells and the hazy appearance due to abundant mucoid material. This woman was delivered of a male infant.)

H.E.N.
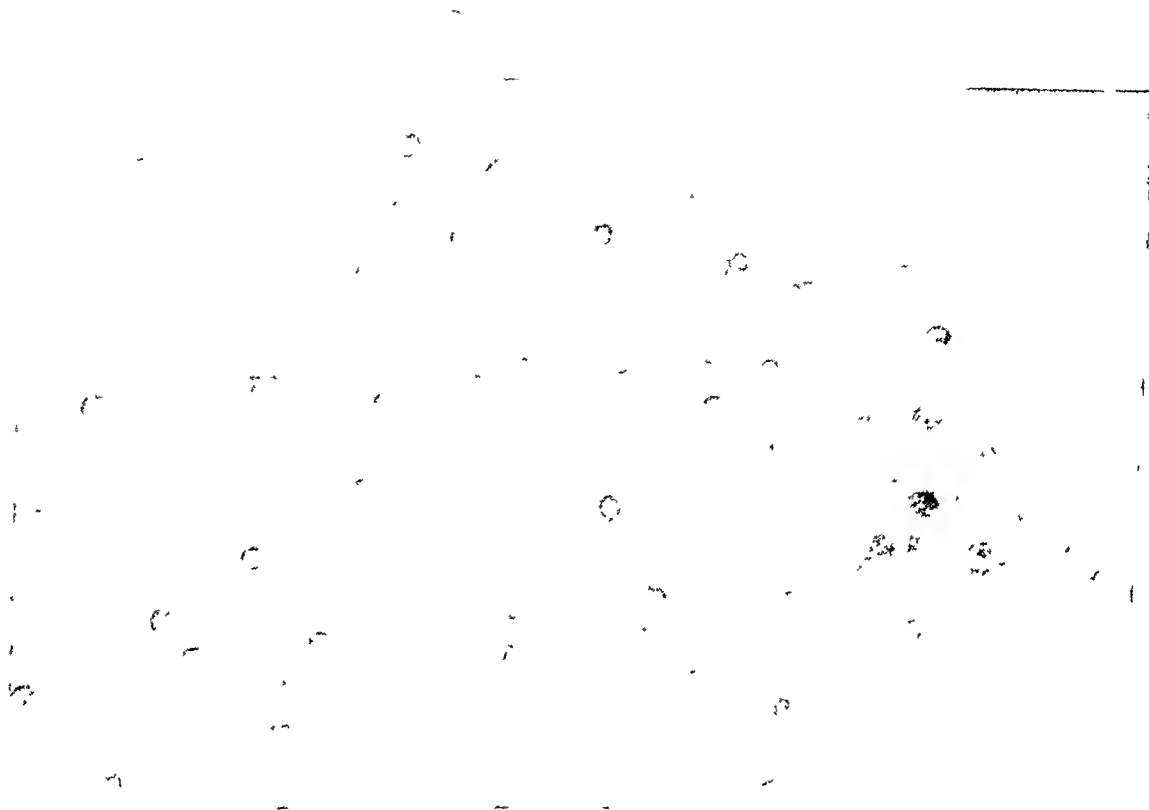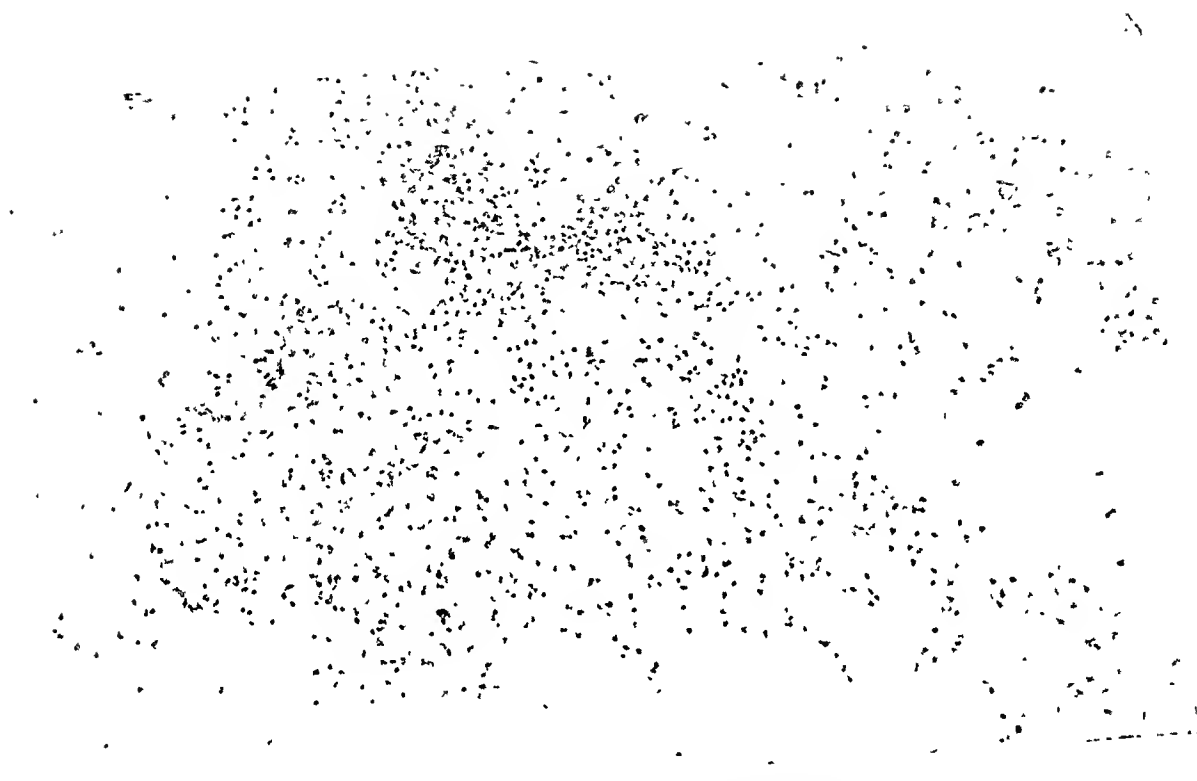
FIG. 4. Cytolytic smear (Low power).
(Note complete destruction of cellular cytoplasm without affecting the nuclei.)

H.E.N.
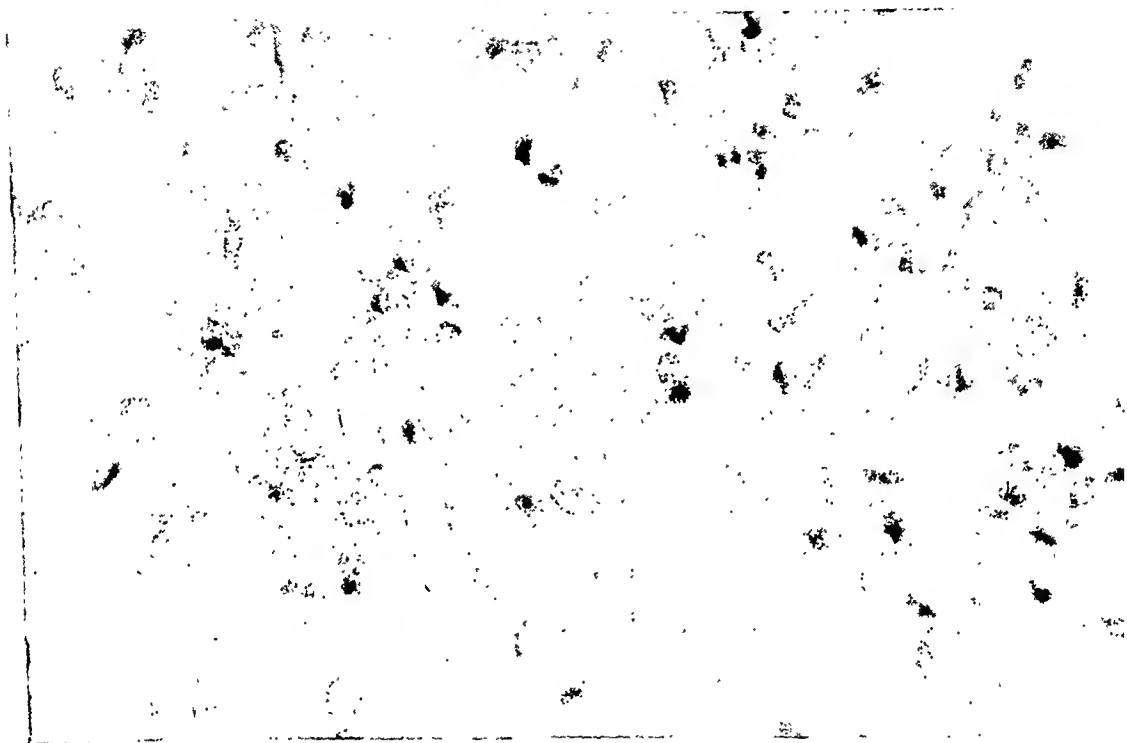
FIG. 5. Cytolytic smear (High power).
(Note complete destruction of cellular cytoplasm without affecting the nuclei.)

H.E.N.

Bilateral Ovarian Dermoids in a Girl of Twelve

BY

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Ovarian dermoids are not commonly found before puberty. Mayo and Butsch (1938) reviewed all the ovarian tumours in girls up to 17 years that had been seen at the Mayo Clinic. The total number of tumours was 16, and of these 4 were dermoids.. None of these was mentioned as bilateral. Wakeley in 1933 said that 7 per cent of ovarian tumours were dermoids, but that dermoids are rarely met before puberty. He described 3 patients aged 8 and 9 years, and in none of these was the condition bilateral. Linn and Ragins (1941), in a review of 103 cases, found that 5 of the patients were under 14, and the youngest was 5 years old. It is not stated whether any of these had bilateral tumours. Koucky (1925), in reviewing 100 cases, found the youngest patient of the series to be aged 18. Pigné (quoted by Miller, 1937), however, records a series of 43 ovarian dermoids and 5 of the patients were under 12 years of age.

Writers have found varying proportions of bilateral cases of ovarian dermoids. Miller (1937), reviewing 953 cases, states that 15.2 per cent were bilateral. Linn and Ragins (1941), give 8.1 per cent as bilateral in their series of 103; Koucky's figure is 13 per cent in 100 cases, whereas Campbell in 1917 gave 1 per cent without giving the size of his series.

The following case seems to be unusual in view of the age of the patient, and the fact that the tumours were bilateral.

CASE HISTORY.

A girl aged 12 years was admitted to Horton Emergency Hospital complaining of intermittent attacks of abdominal pain and vomiting for 3 months. Vomiting preceded the pain and, during an attack lasting several days, both vomiting and pain recurred eac day. The pain was colicky and situated at first in the centre of the abdomen. Later, it had shifted to the right iliac fossa. At the time of admission she had not had an attack for 6 weeks. Her appetite had been poor, but had recently improved. Micturition and bowel action were normal. She had not yet commenced menstruating.

On examination she was found to be well nourished and normally developed for her age. Her cardiovascular, respiratory and central nervous systems were normal. Her abdomen appeared normal, but on palpation an ill-defined mass was felt just rising from the pelvis in the midline. The vulva was normal, and the vagina perforate. *Per rectum*, a smooth, spherical mass almost filling the pelvis was felt behind her small, mobile uterus.

A laparotomy was performed under general anaesthesia, with a midline subumbilical incision. On the right, a pedunculated ovarian cyst, 4 inches in diameter, was found, and removed by dividing and ligating the pedicle. (No ovarian tissue was recognizable, so none could be conserved.) On the left, the ovary contained several retention cysts, and a larger cyst, ¾ inch in diameter. The left ovary was incised, and the larger cyst, together with a few of the smaller ones, was removed, leaving about a quarter of the ovary. The abdomen was closed in layers after an examination of the pelvis had shown no more abnormalities. The patient made an uneventful recovery.

F

Pathological Findings.

Macroscopically. The right ovary contained a cyst, 2½ inches in diameter, unilocular and full of clear, yellow fluid. There was also a cyst, 1¼ inches in diameter, with a thicker wall, and a nodule of solid tissue at one side. This cyst contained a tangled mass of hair and sebaceous material.

In the material taken from the left ovary was a small quantity of normal ovarian tissue, several retention cysts, and one thick-walled cyst, ¾ inch in diameter, full of sebacious material.

Microscopically. The wall of the right dermoid showed a stratified, squamous epithelial lining. Accessory skin structures were present: hair follicles, sweat glands, and sebaceous glands. The lumen contained keratinous material and hairs.

The left dermoid cyst consisted of a fibrous tissue wall lined by stratified squamous epithelium. Accessory skin structures were not present. Flaked-off keratin lay in the lumen.

SUMMARY.

A case of bilateral ovarian dermoids in a child of 12 is described.

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Note of a case of Cerebral Haemorrhage occurring early in Pregnancy

.BY

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THIS case is recorded for two reasons. Cerebral haemorrhage occurring early in pregnancy without obvious cause is a rare condition; secondly it is interesting from the diagnostic point of view.

LITERATURE.

Cerebral haemorrhage during pregnancy has been described under various headings:

1. Eclampsia with convulsions.
2. Eclampsia without convulsions.
3. Cardiovascular renal disease.
4. Uncertain cause.

This case falls into the last group.

The first report of a similar case was made by Mondy of Glasgow who, in 1903, described a case of a single woman 6 months pregnant, who had fits without albuminuria. Accouchement forcé was performed and the patient died a few days later. Lumbar puncture and postmortem details are not given. He described the case as follows: "The peculiar features of this case were the absence of albuminuria . . . and the complication of hemiplegia. During the whole time she spoke only once, and that in answer to my enquiry if she had any pain. There was no oedema anywhere, but her face seemed somewhat puffy."

In 1904 von Hösslin made an extensive survey of all types of paralysis occurring in pregnant women. He found 32 cases of cerebral haemorrhage associated with toxaemia of pregnancy, and 27 cases of cerebral haemorrhage without toxaemia. In this group of 27 cases a further subdivision was made, 10 cases were associated with vascular disease, and in 17 cases no cause for the cerebral haemorrhage was found.

In recent literature, 6 more similar cases are recorded, but 3 of these case reports are not available at present because they were published in Germany during the recent war. The other cases are as follows:

Wagner (1936) reported a case of a primigravida, 28 years old, who was 7 months pregnant. There was a sudden onset of fits and hemiplegia. Urine and blood-pressure were normal. Lumbar puncture was not performed. The patient made a good recovery and was delivered at term by Caesarean section of a healthy infant. The lesion was considered to be a cerebral haemorrhage for which a cause was not found.

Apajalahti (1938) described a case of cerebral haemorrhage in a primigravida, 38 weeks pregnant, aged 30. She started with epileptiform fits, hemiplegia, and aphasia. Toxic symptoms and signs were not found. The patient made a good recovery and had a normal delivery. Lumbar puncture was not performed.

Paucot and Gellé (1938) recorded a case of a 14-para, aged 43, with Wassermann reaction positive. She was 8 months pregnant. Postmortem Caesarean section was performed and a living foetus delivered. There were no signs or symptoms of toxaemia.

CASE HISTORY.

Mrs. H. A., aged 21, primigravida, 5 months pregnant, was admitted to St. Alfege's Hospital on February 1st, 1947, under the care of Mr. Alistair Gunn.

Past history. She had measles when 9 years old.

Menstrual history. Menstruation started at 14 years. Periods were regular and painless. The patient suffered from headaches, accentuated before menstruation. She was known to have an irritable temper; otherwise she was described as healthy.

Family history. Neither of her parents had hypertension. Her brother and sisters are all healthy.

Present history. Last menstrual period was on September 2nd, 1946. She had some sickness during the first 3 months of pregnancy, but otherwise was well. The present illness began suddenly on the day of admission to the hospital, with vomiting and severe headache, while the woman was cooking her husband's breakfast. She collapsed, lost consciousness, and there began a succession of convulsive seizures. The doctor who was called in sent her to hospital immediately.

On admission, the patient was comatose, had stertorous breathing and was having epileptiform fits. Her cheeks were flushed, and she had mild pallor of the conjunctivae. She was well developed, of average height and weight. There was no oedema. Temperature 99°F., pulse 80, respirations 24.

Cardiovascular system. Nothing abnormal was detected. Blood-pressure 120/90.

Lungs. Few rhonchi in both lungs.

Breasts. Active.

Abdomen. The fundus uteri was at a level corresponding to a 22 weeks' gestation. Foetal heart was heard.

Fundus oculi. The discs and retinae appeared normal except for congestion of the veins.

Central nervous system. The patient was deeply comatose. The pupils were pin-point (possibly due to the effect of morphine gr. ¼ given on admission), with sluggish reactions to light.

Reflexes. Plantar extensor; knee jerks exaggerated. She was able to move all her limbs, muscle tone was equal on both sides. Neck resistance was increased and the Kernig sign was positive.

Lumbar puncture. Cerebrospinal fluid was deeply blood-stained, pressure increased.

Urine. No abnormal constituents present.

Blood. Wassermann and Kahn reactions negative.

A tentative diagnosis of sub-arachnoid haemorrhage was made.

Progress. February 2nd. Less deeply comatosed; no further fits; vomiting and incontinent of urine; temperature, 99°F.; pulse 80.

February 3rd. Patient now stuperose but can be roused to answer simple questions; slightly restless. Urinary output cannot be measured due to the incontinence.

February 4th. One epileptiform attack occurred, mainly right-sided. Temperature 103°F.; pulse 90; respirations 20. There were incontinence of urine and faeces, and deep coma. Glucose saline given rectally. Urine: normal.

February 6th. Consciousness was regained after 3 days of coma. Several epileptiform fits, mainly right-sided, were followed by coma.

Lumbar puncture: The cerebrospinal fluid was mixed with blood, and the pressure could not be measured, but it had to be drawn off by syringe.

February 7th. Deeply comatose, flaccid paralysis of right arm and leg. Plantar reflexes R>L. Kernig's sign absent.

The patient was seen by Mr. C. G. Knight, the neuro-surgeon, whose report was as follows:

" The patient was conscious on Wednesday and then appeared to have a second haemorrhage. Right hemiplegia developed, whereas before there was right-sided Jacksonian epilepsy. This suggests a deep extension from a cortical haemangioma, or possibly a middle-cerebral aneurysm."

He advised ligation of the internal carotid artery in the left side. This was performed under local anaesthesia by Mr. J. Gabe on February 7th.

The patient remained unconscious, had no more fits, and died 8 hours later.

Postmortem Examination.

Heart. Cloudy swelling of myocardium of left ventricle.

Lungs. Haemorrhagic bronchopneumonia.

Kidneys. Cloudy swelling and slight fatty changes.

Pelvis. Uterus enlarged, contained five-months foetus. Corpus luteum seen in left ovary. No pathological changes were seen in the uterus or foetus. Placenta was normally inserted, and no retroplacental clot seen.

Brain. Great oedema and congestion. There was an area of recent infarction 7 cm. in diameter in left parietal lobe and slight fibrinous meningitis over it. Another 3 cm. area with fibrinous infarction over posterior part of basal ganglia.

Recent haemorrhage in posterior part of corpus collosum and left lateral ventricle. A little ante-mortem thrombus seen in left middle cerebral artery. No evidence of congenital aneurysm found.

Microscopic Examination

1. Margin of recent haemorrhage in posterior wall of left ventricle.

2. Fibrinous purulent leptomeningitis over haemorrhagic infarction of left parietal lobe of brain.

3. Haemorrhage in and around telangiectasis of veins in posterior part of left basal ganglia.

Summary of Lesions.

Cerebral haemorrhage.
Thrombus in left middle cerebral artery.
Infarction of brain.
Pregnancy 5 months.

DISCUSSION.

Congenital aneurysm, syphilic vascular disease, blood dyscrasias, particularly haemophilia and leukaemia, and diabetes are contributory causes of cerebral haemorrhage of pregnant or non-pregnant women.

Irish (1939) in a study of 1,000 post-mortem examinations of cases of vascular encephalopathy, found cerebral vascular involvement in young subjects in 40 cases. Embolus appeared in 10 cases, thrombus in 6 cases, and haemorrhagic lesions were present in 24 patients under 20 years of age. He mentions that spontaneous cerebral haemorrhage has been found frequently occurring in young people without apparent cause, but careful investigation in some instances has disclosed a small heart and vascular hyperplasia in the cerebral vessels, the so-called "thymic syndrome."

Diseases not peculiar to pregnancy, such as hypertensive cardiovascular and renal diseases, are frequently complicated by cerebral haemorrhage. Parks and Pearson (1943), in a survey of 1,009 cases of toxaemia of pregnancy, found that the total maternal mortality from cerebral complications was 8 cases and, of these, hypertensive cardiovascular renal disease accounted for 3. He also states that chronic hypertensive vascular disease preceded the development of toxaemia; and cerebral haemorrhage occurred in 3 out of 4 fatal cases of eclampsia.

Cerebral haemorrhage associated with toxaemia of late pregnancy is relatively infrequent, but of importance because it is usually fatal. Factors which may lead to rupture of cerebral vessels in toxaemia of pregnancy are: changes in the arterio-capillary walls due to spasm, oedema ischaemia and the vascular changes of persistent hypertension. Parks and Pearson (1943), in their study of 1,009 cases of toxaemia of pregnancy had 41 cases with typical eclamptic convulsions, and fatal cerebral haemorrhage occurred in 4 cases.

Cerebral haemorrhage early in pregnancy is a very rare condition. In cases where no obvious cause exists, Besse (1937) states that vascular damage occurs from autointoxication due to some substance circulating in pregnancy.

von Hösslin (1904) suggests that there is a diminution in the resistance of the vessel caused by cholesteraemia present in pregnancy. The cholesterol metabolism has

some considerable influence on the tone of the endothelial cells and on the thickness of the wall. These variations may lead to angiospasm and later to vascular haemorrhage.

Early recognition of such cases may sometimes save the patient's life, if the appropriate treatment is given. In the above case, there was no evidence of toxaemia or of arterial disease in the brain, and no miliary aneurysm. An early ligature of the internal carotid might have saved the patient's life, although at the cost of some impairment of her subsequent health and happiness.

SUMMARY.

1. A case of fatal cerebral haemorrhage occurring in a patient 5 months pregnant is described.

2. No cause of the haemorrhage was found.

I have pleasure in acknowledging my thanks to Dr. B. A. Young, Medical Super-intendent of this hospital, for his permission to publish this case, to Mr. A. Gunn for his kind advice, and to Dr. Gottlieb for his help and keen interest.

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Fig. 2.

Lateral radiograph of pelvis showing angulation of sacrum.

Fig. 1.

Radiograph of pelvic brim showing trifoliate shape.

S.F.H.

Pelvic Contraction due to Idiopathic Steatorrhoea

BY

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E.C.1.

IN idiopathic steatorrhoea there is an inability to absorb fat efficiently from the intestine. Thus the disease bears a resemblance to other diseases of this type and has been called "non-tropical sprue" and "adult coeliac disease." As a result of the deficient absorption of fats vitamin D is not available and, in addition, there may be poor absorption of salts. The low-fat diet used in the treatment of this disease is poor in calcium content. Thus the bones of the body may be decalcified, giving a picture similar to that of osteomalacia.

Osteomalacia is regarded by many as an adult form of rickets. The underlying cause of the skeletal changes is the same although the age at which it operates is different. This accounts for the difference of the rachitic type of pelvis and the osteomalacic type. In the sitting child the ischial tuberosities are subjected to more pressure than in the adult where pressure is also transmitted through the heads of the femurs with a resulting compression of the sides of the pelvis. In idiopathic steatorrhoea the same factors come into play and if the patient becomes pregnant the same difficulties of pelvic obstruction arise in both diseases.

Only 2 cases of a similar nature are reported in the obstetric literature as occurring in this country. This is probably not because they do not occur but that they are not reported. Kenny (1941) reported a case of osteomalacia in an Indian woman who had come to this country with her husband 6 years before the disease became virulent. This patient had a high blood-calcium level, and therefore (according to S. L. Simpson, 1941) was probably not suffering from true osteomalacia. MacLennan (1944) reports a single case occurring in Glasgow. This was apparently due to poor conditions and food. He could only find one other case in hospital records in Glasgow. From this fact and the fact that rickets is very common in that city he thought that it was unlikely that osteomalacia and rickets had the same aetiology.

The effect of pregnancy in these women is to drain the bones of even more calcium to supply the foetus with its requirements. The bones in these cases may become extremely soft and pliable (Illingworth and Dick, 1945). It has been suggested that this calcium drain is a cause of restlessness and pain in the pelvis, back and thighs associated with violent movements of the foetus (Browne, 1944).

In the case described below, the condition was diagnosed some time before pregnancy occurred and the bones were well calcified at the time of delivery.

Case History.

Mrs. C. B., born 1913.

The patient was first seen at St. Bartholomew's Hospital in May, 1938. She was then complaining of a limp and low backache. These had both started 2 years previously and there had been loss of weight and weakness for the same time.

Examination revealed restricted movements of the right hip, obliteration of the lumbar curve and

a stiff spine with restricted movements. The teeth were good. The urine was normal. X-rays showed generalized osteoporosis with biconcave vertebral bodies, narrow hip-joint spaces and a trifoliate pelvis.

There was no past history of rickets but there had been difficulty in feeding as a child.

On May 21st serum-calcium was 8.7 mg./100; serum-phosphorus 1.4 mg./100 ; Wassermann and Sigma reaction negative. Further investigations revealed haemoglobin 50 per cent; renal function normal. Plasma-phosphatase 0,3 units (normal 0.1–0.2).

Faecal fat: split 24.4 g./100 (71.1 per cent); unsplit 10.4 g./100 (28.9 per cent). Total 34.8 g./100.

Daily average calcium excretion: faeces 428 mg.; urine 13 mg.

Blood-sugar curve was normal. There were no calcified mesenteric glands on X-ray and a barium series revealed a normal intestinal tract.

The patient was treated with total daily doses of calcium lactate, gr. 90; radiostoleum, m. 30; ferrous sulphate, gr. 9; multivite capsules 6.

In September, 1945, the patient was readmitted as an emergency after a short febrile illness. Her haemoglobin had fallen to 16 per cent, leucocytes, 3,300. Treatment with transfusion was successful, 9 pints of blood being given in all. In October, 1945, blood calcium was 10.2 mg./100, phosphorus 2.8 mg./100, alkali-phosphatase 8 units.

The monthly periods were irregular but the patient was seen on October 17th, 1946, when 24 to 26 weeks pregnant; the expected date of delivery being in February 1947.

External pelvic measurements were: interspinous 8 inches, intercristal 11 inches, external conjugate 8 inches.

The pelvic outlet was reduced and the sub-pubic arch narrow. The pelvis was obviously beaked. Vaginally the whole pelvis gave the impression of being reduced in capacity. The X-rays confirmed this and showed the typical trifoliate brim and sharply angulated lower sacrum and coccyx (Figs. 1 and 2).

The pregnancy advanced steadily although the presentation was unstable and was frequently transverse. It was decided to admit the woman near term and perform an elective Caesarean section. She went into spontaneous labour on February 8th, 1947, and a lower segment operation was performed 2 hours later. A living male child of 7 pounds 14 ounces was delivered as an extended breech. The puerperium was satisfactory apart from mild postoperative bronchitis. Breast feeding was not allowed and lactation inhibited by hexoestrol dipropionate 15 mg.

Serum calcium was 9.2 mg./100 on February 27th.

The patient was seen again on April 21st and was well. The baby was 10 pounds 1 oz.

I would like to thank Mr. Donald Fraser for allowing me to look after this patient.

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FIG. I.
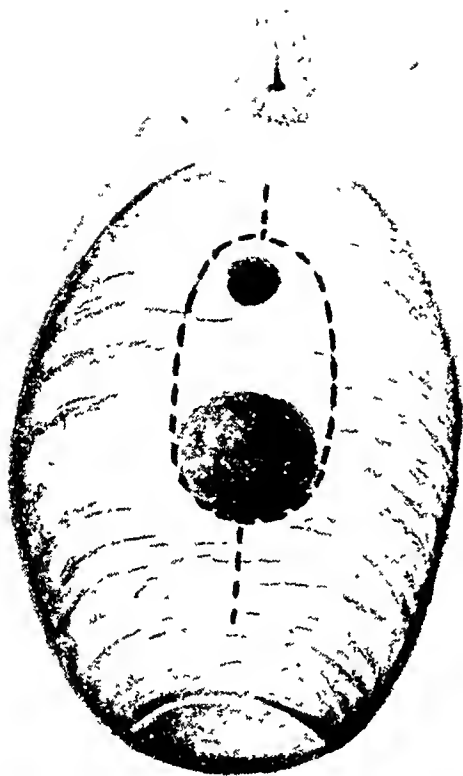
Illustrates the type of vesicovaginal fistula
and line of incision.

B.T.
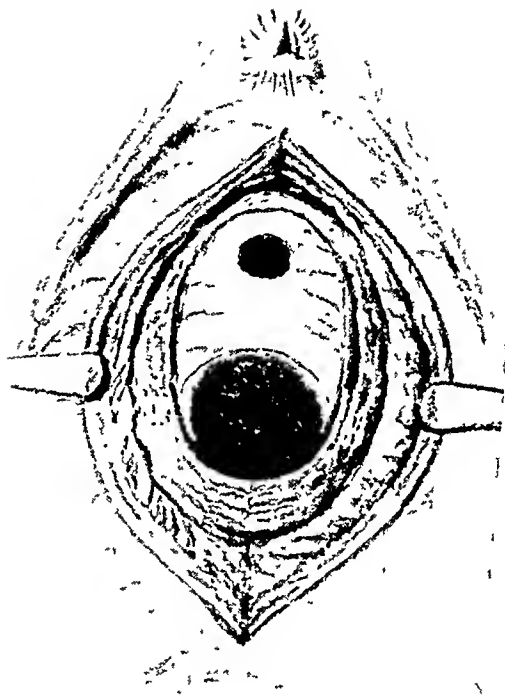
FIG. 2.

Flaps have been raised and the bladder
mobilized.
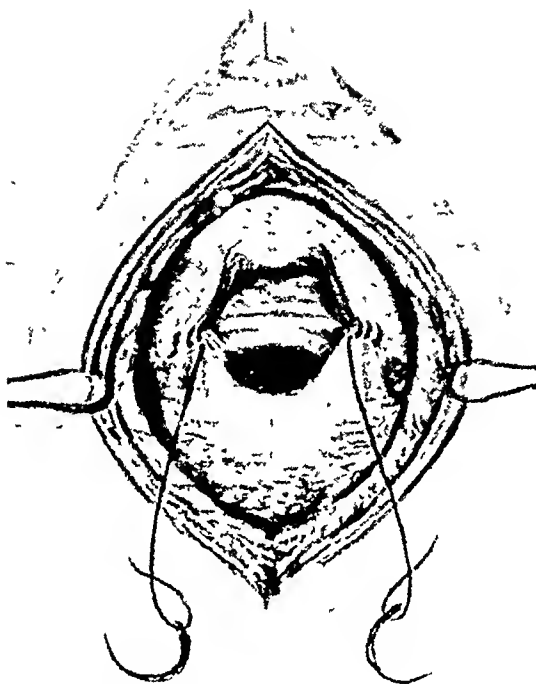
FIG. 3.

Suturing has started from each side. The upper edge of the fistula is being drawn down towards the lower part of the vaginal skin left surrounding the top of the urethra. This vaginal skin is here shown a little dissected up and turned to meet the top of the fistula, thereby obscuring slightly the top of the urethra.
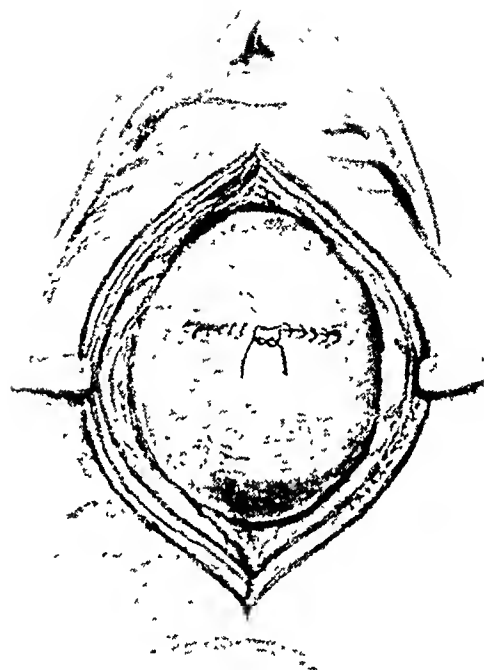
B T.

FIG. 4.

Suturing is complete. The lateral flaps will now be closed over the repair.

Treatment of a Type of Juxta-Urethral Vesicovaginal Fistula

BY

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In a previous communication (Thomas, 1945) I referred to the difficulty of closing a juxta-urethral vesicovaginal fistula when the bladder and the top of the urethra open separately into the vagina. Joan Thompson (1945) mentions the same problem. Frequently the urethra is some $\frac{3}{4}$ to 1 inch in length before it opens into the vagina; the lower border of the fistula may be as much as $\frac{1}{2}$ inch above this, the intervening space being continuous with the vaginal skin. The fistula may be any size, but $\frac{1}{2}$ to 1 inch is common.

The problem is to anastomose the large fistula to the small orifice which the top of the urethra presents. The technique now to be described has been successful in a small series of 5 cases, and since such cases are not uncommon amongst vesicovaginal fistulae (9 out of the 39 juxta-urethral fistulae of obstetric origin which I have so far encountered) I venture to describe it, simple though it is.

The urethra is so thin-walled that if it is dissected out sutures will almost certainly cut through. Further, where a large hole (the fistula) has to be sutured to a smaller one (the top of the urethra) the larger will inevitably pucker and urine will leak. The vaginal skin, however, is much thicker and may be utilized instead of the urethra itself.

The first step is to make an oval incision in the anterior vaginal wall. Its upper border coincides with the upper border of the fistula; at the sides it gradually leaves the margins of the fistula; and below it passes to about $\frac{1}{4}$ inch inferior to the upper orifice of the urethra (Fig 1). Two straight longitudinal incisions are also necessary: one from below up to the lower border of the oval, the other from the upper border of the fistula towards the cervix. Dissection as described previously (Thomas, 1945) now provides 2 lateral vaginal flaps. Deep to these flaps are the bladder with its fistulous opening, the upper end of the urethra, and the intervening vaginal skin still left adhering (Fig. 2).

The bladder must be mobilized freely, particularly from the cervix, until the upper border of the fistula can be pulled down to the lowermost piece of vaginal skin surrounding the urethra. Until this is possible without the slightest tension it is futile to start suturing. Very free mobilization is therefore essential.

Suturing begins at the middle of the long side of the oval, and it is often an advantage to start with a stitch from each side which will meet later in the midline. The upper border of the fistula thus comes to be sewn to the vaginal skin still surrounding the urethra. An area of vaginal skin remains enclosed and in contact with the urine. The lateral flaps are closed over the repair and the bladder is drained as usual.

In suturing it will be found that the vaginal skin left around the urethra and between it and the fistula is comparatively thick and strong and well able to take sutures. Its lower edge may need to be dissected up for about $1/10$ inch to enable it to curl over slightly to meet the upper

border of the fistula. It has a tendency to curl out of the suture line, so that a little of the epithelial surface shows. This must be prevented by pushing it inwards and regulating the tension of the sutures, failing which a leakage of urine would certainly result.

Prior to my last communication I had had 4 juxta-urethral fistulae of this type. Different ways were tried to close them, including the " saccule operation " which was described. All of these failed at the first attempt; one of these was `cured subsequently; another remained operable but did not return; and the other two had their ureters transplanted.

Since then I have had 5 such fistulae and all closed at the first attempt, although the urethra of 1 is unfortunately incompetent. Although the 2 series are small the contrast is evident and may be ascribed, I believe, to the change of technique and not to coincidence.

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Smellie's Method of Forceps Traction

BY

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ALTHOUGH WILLIAM SMELLIE himself might have been surprised to find one feature of his forceps technique isolated and named after him, the usage is quite an old one. In the prolonged discussions on the use of the forceps which took place in the late nineteenth century, at a time when forceps practice was crystallising and when the respective merits of pure traction and traction combined with leverage were being argued, Smellie was regarded by the disputants as the first sponsor of the combined action of the instrument. In 1877, for instance, Dr. Arthur Edis read a paper to the London Obstetrical Society entitled "The Forceps in Modern Midwifery," in which he gave a description of Smellie's method. This paper is perhaps a convenient starting point because it was Edis, as far as I know, who first definitely stated that the method originated with Smellie. The words of Edis's paper were "Smellie directs the operator to pull the head along from side to side or from one ear of the child to another." Smellie's own words (1767) in his *Treatise of Midwifery* were: "Having secured the blades he (the operator) must take a firm hold with both hands and, when the pain comes on, begin to pull the head from side to side." This wording differs from the version given by Edis who, I think, took the quotation from the edition of Smellie's works published by the New Sydenham Society with commentary by McClintock. In this edition McClintock comments favourably on Smellie's method and describes it in the precise words used by Edis.

A further quotation from Edis's paper may serve to recall the protagonists in the argument between pure traction and traction combined with leverage. Edis goes on to say, "This oscillatory or swinging motion in the use of the forceps has been recommended by most writers on the use of the forceps since the days of Smellie. Dr. Mathews Duncan is strongly opposed to this leverage or pendulum-like movement of the forceps, considering it to be useless and injurious.

"Dr. Barnes believes pure traction to be almost impossible and is equally certain that a gentle and careful leverage enables us to deliver with a greater economy of force and time.

"McClintock confirms this view, believing that the movement in question, when executed with moderation and gentleness, is calculated to favour the advance of the head.

"In my own practice I almost invariably resort to this expedient, and have often succeeded in effecting delivery where efforts at pure traction alone have failed."

It will be noted that Robert Barnes is quoted by Edis as approving the method, and Barnes clearly had devoted much thought to its advantages. In his textbook published in 1885 he writes, "It is more instructive to study these two forces (traction and leverage) together. The forceps is a double lever; each branch is a lever and might be used separately; united, each branch acts as a fulcrum to the other. The lever application of the forceps is strongly denounced but, we think, for want of right

understanding of the question and want of delicacy of touch. Leverage is a force indicated by Nature; it is a most important factor in the natural progression of the head. As the head advances, first one side of the the head is felt a little lower than the other; presently a slight oscillation of the head on its long axis is perceived during its screw-movement, the side that was at first highest coming down a little. The adaptation of the head to the planes of the pelvis is largely effected in this manner. Since it is our business to help Nature by imitating her, it would be folly to reject this force."

" The question then remains, how best to use this force. The reply is, not by violent oscillations, carrying the handles first strongly to one side, then over to the other; not by making a fulcrum against the side of the pelvis at the risk of crushing the soft parts, perhaps of opening the bladder; but by gentle, almost imperceptible, alternate movements, traction-force being exerted at the same time, and making the blades of the forceps act as mutual fulcra, or by making a fulcrum of the forefinger.

" Concurrently with traction, slight alternate leverage movements may be executed by swaying the handles gently from side to side within a moderate angle not exceeding 20 degrees. Care is taken not to press the shanks against the pelvic walls. Each blade is the fulcrum to its fellow."

A very good discussion of the use of the method is given by Galabin in his *Manual of Midwifery*, published in 1886. Galabin recognized more clearly than others that the Smellie method is only suitable to the low forceps operation, or, as he puts it, " only in cases in which friction is the cause of the delay," and continues, "as a rule traction should be steady without any swaying." To find out the cases suitable

for lateral movement Galabin advised that, " in obstinate cases an attempt should be made to push the head back between the pains. When this cannot be done and when moderate direct traction fails, then the leverage effect should be employed." In explaining the way in which the method works Galabin was perhaps the first to draw the obvious comparison with the technique used to extract a recalcitrant cork.

Of the other side of the argument the main protagonist was Mathews Duncan. He stated that a pendulum action is useless and injurious, and this point of view can be readily understood in the light of Duncan's preoccupation with the mechanical aspects of the force exerted on the head by the forceps, and his insistence on the injuries that accompany their improper use, an insistence well shown by his book, *The Female Perinaeum* (Duncan, 1879), in which the various types of laceration are described and classified in far greater detail than is usual, or for that matter significant, to-day.

It is clear that in the main the advocates of pure traction had their way. At the most, later writers give a place to the Smellie technique as one for occasional adoption alone, and do not state clear indications for its proper use. Carlton Oldfield, in his edition of Hermann's *Difficult Labour*, says it may be used in difficult cases. In American, Edgar in his *Practice of Obstetrics* published in 1911 stated, " Leverage was once applied more freely than at present. Its principal use to-day is in cases in which the head is advancing with unusual difficulty, when traction may be varied by horizontal to-and-fro movements. The axis of the forceps should not depart more than 30 degrees from the medium plane of the pelvis."

It is interesting to speculate on the

reasons why the method dropped out of use and teaching. Perhaps the powerful antagonism of such men as Mathews Duncan was one reason. After all, in another sphere, namely the induction of labour, the influence of the giant Victorians was powerful enough to supress rupture of the membranes as a commendable method for almost 50 years. The main reason, however, why pure traction gained the day was undoubtedly the general adoption of the axis-traction forceps. With this instrument, if used as intended, any lateral movement is impossible, the traction rods just rock on the blades or shaft and damage the soft parts. Moreover, the cases for which axis traction was devised are not suitable cases for Smellie's method, which is, as Galabin pointed out, only suitable for low operations in which delay is due to resistance and friction of the soft parts. McClintock, in the Sydenham Society commentary already referred to, pointed out that Smellie's free use of the method depended on the fact that he employed a very short instrument.

The new instrument with its increased power certainly needed new rules but, somewhat illogically, these rules were reimposed on the use of the older forceps. Now that the axis-traction phase of midwifery, in the opinion of many, is passing, or has passed, there would seem again to be some justification for a restrained advocacy of Smellie's method of traction in the low forceps operation. Its employment certainly makes extraction a more gentle procedure and one that I think minimizes perineal trauma.

There is perhaps one further point that might be touched upon. In practice, as one instinctively feels for the path of least resistance, the action of the forceps is more that of a screw, as Robert Barnes in the passage quoted earlier suggests, than a pure side-to-side lever. So that, if any leverage at all is permissible, there can be argued as good a case for oblique leverage in any radius as for lateral leverage. This means that if the principle of Smellie's method is sound and that leverage should be combined with traction, then effective leverage should take advantage of every radius that would facilitate extraction, and if this course be followed, then the head would be delivered by a screw-like movement in which the handles of the blades described a restricted spiral.

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Achalasia of the External Os (or Conglutination of the External Os)

BY

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ACHALASIA of the external os is a primary condition met with in primiparae and multiparae during labour in which the cervical canal becomes effaced or obliterated, but the external os remains closed and, at times, difficult to locate.

Historical survey. Carter (1941) in a comprehensive paper on the condition has revealed that from 1859 there had been "only 28 articles on this subject of which the majority consisted of only a few pages, devoted chiefly to case reports". For further information the reader is referred to his article, but I should like to point out that neither he nor other writers have distinguished primary achalasia from those cases which occur as a result of operations on, injuries to, or inflammations of, the cervix.

Pathology. This is believed to be due to non-relaxation of the circular fibres around the os and is similar to the conditions which occur in the oesophagus and colon producing achalasia of the cardia and Hirschsprung's disease respectively.

Symptomatology. It will be easier to describe a more or less typical case. The patient may have received antenatal supervision, the labour to all appearances is progressing normally, the presentation is normal, the presenting part has engaged and the pains are strong and regular. The general condition of the patient is satisfactory but the labour is lasting longer than expected; so the patient is referred to the obstetrician as a case of delayed labour, either with cause unknown or the absence of the external os is remarked.

At times it is impossible to find the site of the external os, as the following case illustrates. Curtis (1933) writes "certain patients have a congenital stenosis of such high grade that after the onset of labour, and especially after the cervical canal has become obliterated, the os cannot be found either by palpation or inspection. One such patient was a primipara 42 years of age. After several hours of fairly strong labour, a Caesarean section was performed which we thought would simplify the identification of the internal os. (The internal aspect of the external os is meant.) Even then the opening could not be located and the uterus was sewn up. There was not the slightest evidence of lochia for 5 days, during which time the patient complained of severe cramp in the lower abdomen. On the 5th day the cervix opened up and the uterus expelled some clots, followed by a normal lochia." Carter (1941) has described a similar case. The cervix is usually thin, soft and more or less obliterated, or it may be soft and oedematous. The external os after a varying interval of time may dilate and the patient deliver herself spontaneously.

Complications. If for some reason the diagnosis is missed and the patient is allowed to continue in labour, then one of the following complications may occur:

(1) The cervix will become very stretched and attentuated and the head may be born

enveloped in the cervix (DeLee and Greenhill, 1943).

(2) Circular amputation of the vaginal cervix may occur (DeLee and Greenhill, 1943).

(3) Transverse rupture of the anterior wall of the cervix has been reported (Eden and Holland, 1937).

(4) Rupture of the lower uterine segment.

(5) "Missed labour."

Diagnosis. The following points are important:

(1) The history. The cervix has not been operated on and there has been no known cervical disease.

(2) The labour is delayed although the presentation and position may be normal, and the cervix is soft and more or less obliterated.

(3) The external os cannot be located or it is represented by a smooth, slightly depressed, non-resistant circular area, imparting to the finger a sensation somewhat different to the rest of the cervix. According to DeLee and Greenhill (1943), the opening can be seen through a speculum as a tiny hole containing a little mucus, and surrounded by a very red ring. Porter (1910) reported a case in which examination by speculum " revealed a small stream of meconium emerging from a depression in the cervical tissue, through which, when the meconium was wiped away, a few long black hairs emerged ". In one of my cases a tiny drop of sanguineous fluid escaped from the external os on applying pressure to the cervix.

The 2 conditions which may be mistaken for achalasia of the external os are:

(i) Anterior or posterior sacculation of the cervix causing the external os to be displaced posteriorly or anteriorly respectively. A careful examination will reveal this error.

(ii) Stenosis of the external os following operations or injuries to the cervix. The history and the presence of scar tissue will differentiate it.

Prognosis. The prognosis is good provided the diagnosis is made reasonably early.

Treatment. This is simple and effective in the majority of cases and consists in applying firm digital pressure at the site of the external os which yields after a minute or two. The os then rapidly dilates and delivery is uneventful. Cragin (1916) quoted by Curtis (1933) recommends " the use of a sharp instrument to pierce the thinned out cervix where the os should be " but this is not necessary nor advisable. Of course, any obstetrical complication will have to be dealt with on its merits. Carter (1941) had to perform Caesarean section in order to obtain a living baby, because of the delay in the 1st stage. . In one of my cases Caesarean section was performed in the interest of the child. Occasionally Caesarean section has to be employed in cases where the external os cannot be located.

Incidence. It is difficult to assess the incidence of a condition which is not even mentioned in many textbooks, and when mentioned, is confused with stenosis of the external os resulting from operations on, injuries to, or inflammatory conditions of, the cervix. It must, however, be remembered that when a condition is not known it is not thought of and therefore not recognized.

The following 3 cases of my own are illustrative of the condition:

CASE I. Primigravida, aged 35. Afro-West Indian. No antenatal care; admitted 8.30 a.m. on December 13th, 1943. Labour had started at 10 a.m. on December 10th. Pains became stronger on the 12th. The patient was referred to me because the midwife could not locate the external os.

Menarche aged 13; for the past 8 years menses were very scanty. Married for 10 years. Appendisectomy in 1931.

Examination. Well-nourished patient; urine was normal; blood-pressure, 130/80. Pelvic measurements were normal; foetal heart present. Breech presentation.

Vaginal examination. The external os was not made out by palpation. On inspection it was recognized by the escape of a small drop of sanguineous fluid. The cervix was soft, slightly oedematous and almost obliterated. The diagnosis was confirmed by the consulting obstetrician.

At 3.30 p.m. classical Caesarean section was performed and a full-time female child with extended legs was delivered, weighing 7 pounds 6 ounces.

Comment. This was the first case of achalasia of the internal os we had ever seen. We thought Caesarean section was indicated on the grounds of the age of the patient, the duration of labour, and the fact that this was the first pregnancy after 10 years of marriage.

CASE 2. 1-para, aged 28 years. Afro-West Indian; at term; had received antenatal care. Admitted at 11.30 a.m. on June 15th, 1944; in labour for 13 hours. The patient's first pregnancy had terminated in a stillbirth 10 years before.

Examination. Oedema of lower limbs was present; there was perinasal and perioral pigmentation and keratosis. Albumin was present in the urine; blood-pressure, 130/100. The midwife diagnosed a vertex presentation by abdominal palpation but on vaginal examination she thought it was a breech. The case was thereupon referred to me. Abdominal palpation revealed a vertex presentation probably occipitoposterior. On vaginal examination the external os could not be located, but bilateral sacculations with a depression between them could easily be felt, the cervix was soft and oedematous and almost obliterated. The diagnosis of breech was understandable. Inspection confirmed the digital findings. The external os, which was closed, was situated in the gutter between the sacculations. The os was easily dilated, and under chloroform, after overcoming a constriction ring, the head in occipitoposterior

was rotated to occipito-anterior, a volsellum applied to the scalp and a weight of 1½ pounds attached to it. The patient was delivered 8 hours afterwards of a healthy male child weighing 7 pounds. Duration of labour was 25¾ hours. The cervix was torn on the right side. Mother and infant were discharged well.

Comment. This case presented several interesting features, but the occipitoposterior presentation was the most important, and perhaps produced the constriction ring and the oedematous cervix. It is not sufficiently recognized that occipitoposterior positions are the commonest cause of constriction rings.

CASE 3. *Primigravida aged 23 years; Portuguese;* had received no antenatal care; admitted 4.45 a.m. on October 2nd, 1945.

Labour had started at 10 a.m. on October 1st, and as progress was not satisfactory the patient was referred to hospital. Examination revealed blood-pressure 100/50; urine normal; left occipito-anterior presentation. The cervix was obliterated and the external os appeared as a small depression. The external os was dilated up to 1 finger with a little difficulty and a sharp ring " wire rim os ", of resistant tissue prevented further dilatation. Six hours afterwards, at 3.45 p.m., the os was the same size, chloroform was administered and the external os was dilated up to 3 fingers. A healthy male infant, weighing 5½ pounds, was delivered at 5.55 a.m. on October 3rd. Duration of labour was 43 hours 55 minutes.

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WILLIAM GOUGH

Obituary

WILLIAM GOUGH
F.R.C.S., F.R.C.O.G.

WILLIAM GOUGH, Emeritus Professor of Gynaecology in the University of Leeds, died on 29th June, at the age of 71.

He had a distinguished student career at the Yorkshire College, Leeds, winning many prizes. He obtained the B.Sc. London, in 1895, and in 1900 the M.B., B.S., London, and the Conjoint diplomas.

At Leeds University he was Honorary Demonstrator in Clinical Obstetrics from 1911 to 1923 and Lecturer in Gynaecology from 1926 to 1931. He became head of the Department of Obstetrics and Gynaecology in 1931 and was Professor of Gynaecology until his retirement in 1936.

He took the F.R.C.S., England, in 1903, and was appointed Honorary Assistant Surgeon to the Women and Children's Hospital in 1909, being promoted to the full staff in 1919. He became Consulting Surgeon in 1936. He was Honorary Obstetric Surgeon to Leeds Maternity Hospital from 1908 to 1936, and Consulting Surgeon after that until his death.

He was Gynaecological Surgeon to the Leeds General Infirmary from Mr. Oldfield's retirement in 1930 until the end of 1932 when the Infirmary ceased to possess gynaecological beds.

He was made a Foundation Fellow of what is now the Royal College of Obstetricians and Gynaecologists in 1929. He served on the Council of the College from 1937 to 1941 and was elected Vice-President in three successive years, 1942–1945. He attended the Council meetings regularly during the London blitz and afterwards, and did valuable work as Chairman of the Examination Committee in 1944–1945. The College was one of his main interests in later life.

He served in the 1914–1918 war as a Captain in the R.A.M.C. both at home and in France, performing surgical duties.

He was a regular attendant at meetings of the North of England Obstetrical and Gynaecological Society, being as a rule, rather a contributor to discussions than a reader of papers. He was President of the Society in 1926. He also greatly enjoyed his visits to other university centres both at home and abroad with the Gynaecological Visiting Society: he attended the London meeting in May of this year.

William Gough was house surgeon to Mayo Robson—and he became Moynihan's private assistant. A fine training in the golden age of Leeds surgery, and a strong natural bent made him an exceptionally skilful operator; he was completely ambidextrous. The surgical side of his work interested him much more than the obstetric side, but his enjoyment of surgery did not prevent him from being a conservative obstetrician, restraining when necessary

the *furor operativus* of his juniors. He seldom taught, indeed he was very sparing of words altogether, but he was always ready to give a balanced and informed answer to a questioner; when he spoke it was always to the point. He was a wise clinician, and as devoid of bias as it is possible to be: the fairness of his judgment was remarkable. His humanity no less than his skill appealed to his patients.

He married, in 1905, Miss Agnes Crane Fraser who survives him with one son and four daughters. He was exceptionally happy at home, and he was a proud grandfather, always willing to talk of his beloved grandchildren.

BOOK REVIEWS

"The Childbearing Years." By C. Scott-Russell, M.A., F.R.C.S., M.R.C.O.G. Blackwell Scientific Publications, Oxford, 1947, pp. 88. Price 7s. 6d.

Folk-lore revels in the mysteries of reproduction and even in the so-called civilized races much suffering has resulted from the unreasoning acceptance of time-worn dictates. This influence is felt not only among the illiterate.

The author has set out to undo some of the harm that has been done and is still being done by ignorance among women of the facts connected with the reproductive aspect of their lives. He seeks to enlist the help of intelligent, educated, young women by presenting them with an authoritative account of human female physiology and some corresponding pathology. He tells them of menstruation, pregnancy, childbirth and the puerperium, of sterility, contraception and abortion; of the menopause and the disorders of middle age. His information is factual and surprisingly comprehensive considering the quite small size of the book. He has been careful to use language which does not presuppose a scientific or specialised educational background. Given the ability to reason and to weigh evidence the book will be understood easily. It is essentially written for the undergraduate type of young woman. It is to be hoped that his readers will pass this reliable information on to wider circles where ignorance on these matters is often profound.

The book has a pleasing format and contains some very good drawings and radiographs.

"Gas and Air Analgesia." By R. J. Minnitt, M.D., D.A. 3rd edition. Ballière, Tindall and Cox, London. Pp. viii + 80; 19 illustrations. Price 5s.

The third edition of R. J. Minnitt's "Gas and Air Analgesia," although small, is noteworthy for its practical instruction in the administration of gas and air during labour. Dr. Minnitt emphasizes many details in the use of the Minnitt's apparatus which, to the casual reader, might appear superfluous, but to anyone who has supervised and taught midwives to administer gas and air, these simple points are of the utmost importance. The subject matter has not undergone extensive revision but greater emphasis has been laid on antenatal instruction in the use of the apparatus to the patient. The rules of the Central Midwives Board for the giving of gas and air are also plainly set out.

Full description of the practical points will make this book appeal to all who administer gas and air, be it for the relief of labour pains or for minor surgery. The book is well produced and the illustrations are good and instructive. This small book shows us the beginnings of a real attempt to relieve the pangs of labour and great tribute should be paid to Dr. Minnitt as the prime mover in this humane endeavour.

"Introduccion al Estudio de la Plasmoterapia." By Jose M. a Massons, 1947. Editorial "Miguel Servet", Barcelona; 251 pages, illustrated. (In Spanish.)

The author begins his book with a short and lively history of blood-transfusion, tracing its use from fabulous to present times through Graeco-Roman mythology, Hebrew rabbinical writings, mediaeval papal case-histories, to attempts to rejuvenate the Roi Soleil.

The operation seems to have had a sacerdotal aspect in earliest times, therapeutic later (in leprosy of royal personages), aphrodisiac always. The results were sometimes fatal ·to donor and recipient alike; "cross-matching" in 1556 having consisted in selecting a donor of moral character like that of the recipient but of superior physique.

The first obstetrician to advise blood-transfusion in obstetric haemorrhage was Blundell in 1818; he seems also to have observed the ill-effects of

transfusion of one species of animal from another. He is credited with the saving of 6 of 9 desperate cases by transfusion. So down to our own times and the discovery of blood-groups and anticoagulants and the preservation of blood; the indications for its use in infections, shock and haemorrhage being given tragic impetus by the First World War, the Spanish Civil War and the 1939–1945 War when plasmotherapy came into its own to meet the exigencies of a war of movement on far-flung battle fronts. Starting in Germany, plasmo-transfusion more slowly gained popularity in the Allied countries and eventually almost completely replaced the need for blood-banks. All this makes a fascinating story. The bulk of the book is devoted to sober physiopathology. The constituents of the blood, their fractionation, their preservation and clinical application are well described. Under the last, almost every disease process is discussed in relation to blood- and plasma-transfusion and the references to recent literature are abundant and valuable. Several sections are devoted to the technique of administration; the apparatus and possible routes are described and illustrated. A section is given over to the technique of trans-fusion in babies and a last chapter to accidents and their avoidance. This book has no close parallel in the English language and would earn well-deserved popularity in such translation among students and practitioners here.

REVIEW OF HOSPITAL REPORT

THE EIGHTH REPORT FROM THE DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY IN THE UNIVERSITY OF OTAGO, NEW ZEALAND.

This report covers the period from December 1945 to January 1947, inclusive. During this time there were 1,000 confinements resulting in the birth of 1,019 children. The work of the gynaecological department for the same time is also analyzed.

Three maternal deaths (0.3 per cent) occurred in the obstetrical department as the result of eclampsia, obstetric shock, and massive pulmonary embolism. None of these patients had attended the hospital antenatal clinic. There was not a maternal death among the 767 (76.7 per cent) who did attend for antenatal care.

Abnormalities are not a noticeable feature in the practice of this hospital. Toxaemia of late pregnancy constitutes the largest single group of abnormal cases. In this group are 68 patients of whom 58 were considered to have true toxaemia while 9 were considered to be cases of hypertension and 1 of chronic nephritis. The rate of Caesarean section is 3 per cent (30 cases) while the forceps-rate is rather high, 11.3 per cent (115 cases). Breech delivery in single pregnancies occurred 27 times, of which 19 were primigravidae.

In the breech table no attempt is made to separate the results in primigravidae from those in multigravidae. As the only 2 stillborn infants in this group were macerated and the only neonatal death occurred in a premature infant it is possible to deduce that the foetal survival-rate in uncomplicated primigravid breech delivery is 100 per cent.

Of the 1,019 infants in the hospital 957 were full time, while 62 (6 per cent) were premature. In the former group there were 16 stillbirths and 1 neonatal death and in the latter 7 stillbirths and 12 neonatal deaths—a loss of 1.8 per cent of the mature and 30 per cent of the premature infants.

In the gynaecological department 16 deaths occurred among 867 patients. The causes of these deaths are listed but details are not given. This is a matter for regret, as the details of fatal cases can be most instructive. There was only 1 post-operative death—pulmonary embolism following subtotal hysterectomy for fibroids—in 603 cases treated by operation, but of the cases of fatal puerperal sepsis, of acute pneumonia with pregnancy, of cerebral haemorrhage with pregnancy, of encephalitis due to mumps with pregnancy, and of acute yellow atrophy, etc., details are not given.

Only 3 cases of sterility were investigated. Some explanation might have been given for this low figure. Do the women of Otago not complain of sterility or are they investigated entirely as out-patients? The reader is not informed.

ANTHONY W. PURDIE

ROYAL SOCIETY OF MEDICINE.

Section of Obstetrics and Gynaecology.

A Meeting of the Section was held on 28th June, 1947.

RECENT RESEARCHES ON THE PHYSIOLOGY OF MAMMARY DEVELOPMENT AND FUNCTION.

S. J. FOLLEY.

Abstract.

Mammary growth is under the control of the ovarian hormones, oestrogen and progesterone. The exact rôle of each in the stimulation of mammary duct and alveolar growth respectively varies somewhat among different species. In some species, which include the guinea pig, the monkey and ruminants, oestrogen alone evokes both duct and alveolar development. In recent years, striking results on experimental mammary development with synthetic oestrogens have been obtained in farm animals. It has been shown that in virgin goats and heifers, and sometimes barren cows, it is possible in many cases artificially to develop udders capable of producing economic yields of milk. As udder development proceeds, oestrogen stimulation of the pituitary apparently results in the production of the complex of hormones necessary for the initiation of lactation. The responses, however, are rather variable, and in most cases are considerably less than the yields which would have been expected during a normal lactation. This is probably because the alveolar tissue developed under the influence of oestrogen alone is not normal histologically. Experiments in progress indicate that additional treatment with progesterone is necessary to evoke the development of normal alveolar tissue.

Experiments on the stimulation of established lactation (galactopoiesis) as distinct from the initiation of lactation (lactogenesis), have indicated that anterior-pituitary extracts contain a galactopoietic hormone complex capable of evoking considerable increases in the milk yields of cows in declining lactation. Unfractionated ox anterior-pituitary extracts are much more active in this respect, for a given unitage of prolactin, than purified prolactin preparations. It is suggested that clinical trials of such unfractionated pituitary extracts should be carried out in view of the rather variable results obtained in treatment of hypogalactia in women with purified prolactin.

Recent research has also revealed a relationship between the thyroid gland and lactation. Suitable treatment with thyroid hormone has been found to result in marked galactopoietic responses in cows in declining lactation. The discovery that iodoprotein exhibiting thyroid activity when administered by mouth, can readily be prepared by treatment of certain proteins, such as casein, under specific conditions with iodine, may prove to be of considerable practical importance in the dairy industry, since such iodoproteins can easily be administered to cows by incorporation in the ration. In view of the extensive existing knowledge regarding the galactopoietic effect in lactating cows of thyroid preparations, and in particular artificially prepared iodoproteins, clinical trials of such material for the treatment of hypogalactia in women would appear to be justified.

COMPOSITION OF MILK.

Dr. S. K. KON.

Over 2,000 samples of human milk collected in Reading, Shoreditch, Paddington and other localities during 1941–45 were analyzed for vitamin A, carotenoids, vitamin B_1, riboflavin, ascorbic acid, fat, total solids, and some of them also for lactose, total nitrogen, calcium and phosphorus.

The purpose of the investigation was to determine to what extent the composition of the milk

reflects the state of nutrition of the mother and to study the influence on milk of dietary changes brought about by wartime conditions. Factors like time of day, the stage of lactation, milk yield, the age and parity of the mother, were also studied. Small-scale dietary surveys were also done.

The vitamin A and riboflavin content of milk changed but little in the course of the study and there was no seasonal variation. An increase in the vitamin B_1 content accompanied the change from white to national wheatmeal bread.

The vitamin C content fluctuated with the season of the year and the supply of green vegetables, potatoes and oranges.

THE ANATOMY OF THE FEMALE BREAST IN ITS RELATION TO HORMONAL RESPONSE.

S. ENGEL, M.D.

Anatomical and histological investigations have been carried out on some 80 breasts in the resting and active stage. In many cases large sections through whole breasts have been used on account of the variations in any single breast.

It could be shown that the mammary gland in man differs from that of animals. The latter are filled to capacity with glandular tissue when lactating, whereas in man there occur many variations, ranging from almost nil to animal-like abundance. Approximately one-third of the breasts examined proved to be well equipped, about one-third below the average. The remainder showed many transitional stages. Clinical experience regarding lactating capacity is in accordance with the anatomical figures.

Badly equipped, resting breasts show primitive, badly differentiated glands. These glands respond poorly or not at all to hormonal stimulus, as can easily be seen in menstruation. Well or less-well differentiated glands of one and the same organ will show different reaction, that is to say rich sprouting in the first case and nil, or almost nil, in the second. This behaviour accounts for the divided opinion as to the changes of the resting breast in the menstrual cycle, illustrating the fact that women with well-equipped breasts show clinical and anatomical changes, whereas others remain indolent. The conclusion is that menstrual changes in the breast may, or may not occur.

In pregnancy, the development depends on the congenital nature of the breast, since hormonal stimulus cannot do more than mature what is present in the resting breast. The hormonal treatment of hypogalactic women is, therefore, limited, for it can only help to bring the mammary gland to its maximal production; it cannot convert a bad breast into a good one.

In brief, it can be said that the mammary gland in man differs so greatly that its variations must be taken into account when speaking of hormonal influences. The badly equipped breast will not respond at all, or very little, in menstruation. The presence or absence of clinical symptoms in menstruation will serve to estimate and predict the capacity of lactation in individual cases.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

A meeting of the Society was held in Newcastle-upon-Tyne, on Friday, 6th June, 1947.

The President, Professor A. M. Claye, was in the Chair.

Mr. F. J. Burke reported a case of

THECA CELL TUMOUR

The patient was a frail lady of 74 years who complained of an abdominal tumour associated with pain. Five years previously her practitioner had noticed a large hard abdominal tumour, but because of the patient's age he had considered surgery inadvisable. At that time pain was intermittent and tolerable, later it became unbearable, so she was referred to Mr. Burke.

Despite her frailness the patient was energetic, vivacious, and did social work. She had been a spinster until the age of 72 years, and stated that marriage had brought her great happiness.

Menstruation was regular with moderate dysmenorrhoea from 14 to 52 years of age. She had enjoyed good health until the abdominal pain commenced. Marital intercourse and sexual

desire were normal. Slight vaginal bleeding had occurred twice recently, once following coitus.

The pain was in the right iliac fossa. It had been intermittent but became constant with acute exacerbations.

Examination showed a large, hard, rounded tumour almost filling the abdomen. The vulva and vagina were not atrophic. The cervix was high and the uterine body could not be outlined bimanually. Her blood-pressure was 200/110.

A degenerating fibroid was diagnosed and operation advised, but the patient demurred as she did not wish to end her romance on the operating table.

Operation revealed a large rounded tumour arising from the right ovary free from adhesions; but the caecum was densely adherent to the posterior abdominal wall and the pedicle of the tumour. Apparently movement of the tumour distorted the caecum and caused pain. The left ovary was atrophic but the uterus was not. There was no ascites. The tumour was removed. A fusiform aneurysm of the right common iliac artery was noticed.

Convalescence was uneventful. Two months later she reported that she had been rejuvenated but that she was having a second menopause. There was no vaginal bleeding following operation.

Pathology.

The tumour weighed 20 pounds, and was nearly round. It was hard except where two cysts were present. The cut surface was white with a golden tinge and there was a suggestion of lobulation. It was difficult to cut and was free from degeneration. The 2 cysts were 3 to 4 inches in diameter with smooth walls. One contained effused blood and the other golden yellow fluid.

Sections showed a uniform pattern with prominent branching bundles of connective and hyaline tissue enclosing islands of small cells with dark staining nuclei resembling fibroblasts. Some areas showed more epitheloid-like cells. Vacuoles in a few cells suggested the presence of lipoid material. The histological picture was that of a theca cell tumour.

Mr. Burke commented that he had no doubt the tumour belonged to the theca cell group, although staining for lipoid and fibrillary processes,

also hormonal assay of the tissue and endometrial biopsy was not done.

He thought this the largest theca cell tumour so far described. Nevertheless the hormonal effect was slight as it was probable that there was little hyperplasia of the endometrium. Smaller tumours have shown marked hyperplasia with repeated bleeding, but in this case slight bleeding occurred on 2 occasions.

Discussion.

Dr. Newton mentioned a case of post-menopausal haemorrhage where the ovaries looked normal but the pathologist found a plate of theca cells.

Mr. Stabler thought that the case mentioned by Dr. Newton should not be classed as an ovarian tumour—a plate did not mean a tumour.

Mr. Snaith wondered if any one had seen a case of postmenopausal bleeding after bilateral oöphorectomy. He had seen a case associated with an ovarian fibroma.

Dr. R. Morison said he had seen 2 cases, and emphasized the difficulty of pathological diagnosis.

Mr. Corbett wanted to know if this woman would have got married if she had not had this tumour.

Mr. Burke in reply said that many people thought that theca celled tumours should not be separated from granulosa cell tumours. He thought she would not have married if she had not had the tumour. He was impressed by the fact that her late marriage was the great event of her life, and, since the tumour had been removed, he was apprehensive about meeting her again!

Mr. Burke also reported a case of

INGUINAL ENDOMETRIOMA

The patient, age 44 years, had one child 6 years old delivered by lower segment Caesarean section. Four months later she noticed a swelling in the left groin, which gradually increased in size and was painful during and after menstruation.

Examination revealed a linear hard tender mass extending from just above the inner end of of Poupart's ligament to the upper part of the vulva. Mobility was restricted but it was not attached to the skin. Further examination was negative.

Operation revealed an ill-defined cord-like mass which extended through a wide external abdominal ring and was traced to the round ligament above. The lower end tapered into the labium. It was densely adherent to all adjacent tissues. The round ligament was severed and allowed to retract, and the external ring tightened.

Pathology.

The specimen was 2½ inches long and ½ inch thick. It was hard and nodular and contained several small cysts lined with a shiny membrane containing watery fluid. The hard nodules consisted of fibrous tissue and the cut surface showed haemorrhagic spots and exuded chocolate material.

Section showed muscle and fibrous tissue, cystic spaces lined with flattened cubical and and columnar epithelium and areas of menstruating endometrium.

The speaker said that the first case of inguinal endometrioma was described by Cullen in 1895. Less than 50 cases had been recorded in the literature.

Not infrequently the condition had been mistaken for hernia. Usually it had taken 6-8 years to develop to the size of a walnut. Blumer observed a case for 27 years, but most cases had been operated on in their late thirties. Usually relative infertility had been associated even in cases where no intrapelvic endometrioma co-existed. In many of these cases the inguinal endometrioma was a direct extension from a pelvic mass. The interest in this present case and in some others was that there was no evidence of endometrioma elsewhere.

Mr. Burke thought there were 5 possible explanations of inguinal endometrioma :

1. Implantation which was only possible if a hernia or a patent canal of Nuck existed.

2. Direct extension along the round ligament from a focus in the pelvis.

3. Metaplasia of serosal epithelium.

4. Metastases by blood or lymph channels.

5. Müllerian cell rests.

In this case the first 2 explanations could be ruled out. Metaplasia was a possible explanation and embolic spread had been proved. The fact that this type of endometrioma affects the round ligament, which in early development is closely related to Müllerian duct, inclined him to the view that the Müllerian cell rest theory is the most probable explanation of inguinal endometrioma.

Discussion.

Prof. Farquhar Murray asked if implants had been recorded after curettage by the abdominal route following myomectomy.

Dr. Stanley Way said he had seen such a case.

Prof. Jeffcoate stressed the necessity for wide excision. He thought the serosal cell metaplasia theory more likely than the Müllerian rest.

Mr. Harvey Evers said he had seen a· case following myomectomy and Caesarean section and had removed a uterus in one piece with the scar endometrioma to which it was attached. He had operated on a small inguinal endometrioma which was adherent especially in the deeper part.

In reply Mr. Burke said he agreed that there may be more than one original but he thought it easy for a cell rest to get to the inguinal canal. He had seen two cases of scar endometrioma and mentioned that it occurs in appendicectomy and other scars where the genital organs have not been touched.

Professor Farquhar Murray described a case of

RETROVERTED GRAVID UTERUS AT TERM

and read a short communication on

A DIFFICULT DILATATION.

A multipara, in her thirties, was seen early in pregnancy. Examination revealed nothing abnormal. Professor Murray was asked to see her again some months later, when he found the breech presenting and on pelvic examination what appeared to be a fibroid.

Classical Caesarean section was done just before term. The placenta was anterior. Routine palpation of the os was done. It could not be found, but the operator realized his hand was in the " fibroid ", Meantime the patient was bleeding profusely and a rapid decision to do hysterectomy was made. The cervical canal was found squeezed tightly against the back of the symphysis. The mother and baby did well.

Professor Murray was impressed because the placental site bleeding must have been similar to that which occurs in placenta praevia postpartum due to the thinned out muscle tissue which has to control the bleeding.

Discussion.

Professor Claye said that sacculation was a source of error in diagnosis. There had been one case in Leeds.

Mr. Harvey Evers mentioned a case described by Professor Lyall. The patient was 8 months pregnant and the uterus was prolapsed outside the vulva. She died of renal complications.

Professor Murray and Mr. Corbett both mentioned cases following ventrofixation of the uterus.

Professor Murray remarked that most dilatations were straightforward and easy, but occasionally there was difficulty at the internal os usually in cases of dysmenorrhoea with an anteflexed uterus. By curving the flexible tip of a uterine sound the difficulty might be passed, but it was not possible with the more rigid dilators.

Ultimately Professor Murray hit on a technique which he has found invariably successful. He dilated the cervical canal as far as the internal os up to a No. 8 Hegar dilator. Then he reverted to a No. 1 Hegar and invariably was able to negotiate the passage and complete the dilatation.

Mr. D. Flett Smith read a paper on

POST-MENOPAUSAL HAEMORRHAGE.

An analysis of a year's consecutive admissions to the Royal Victoria Hospital Newcastle-upon-Tyne (May 1946 to May 1947).

A period of one year after the last menstrual flow was taken as a minimum time before the case was labelled one of post-menopausal haemorrhage.

There were 147 such cases and their average age was 58.7 years. Sixty-five cases (44.2 per cent) were due to a malignant condition. This figure is lower than that recorded in most publications.

The commonest single cause was carcinoma of the cervix—46 cases or 31.3 per cent. Of these, 37 cases were of the epidermoid type, 4 were adenocarcinomata. In 1 case both types were present; 4 cases were not biopsied because of their advanced stage. Of the 37 squamous-cell carcinomata 30 were non-keratinising and 7 were keratinising. The average duration of symptoms was 7 to 8 months. The average age of this group was 57.7 years. Forty-four were parous women; and average parity was 5.3 children. Two cases, or 4.3 per cent, occurred in nulliparae. Two cases occurred in a cervical stump. One case was a recurrence following vaginal hysterectomy for carcinoma

of the cervix 22 years previously. Three cases were recurrences following radium treatment.

There were 13 cases (8.3 per cent) of carcinoma of the body. Their average age was 55.4 years, and 10 were parous (1 had had 8 children, 2 had had 4, 3 had had 2, and 4 had had 1). The average duration of symptoms was 1½ years.

Microscopical examination showed:

7 adenocarcinomata.
2 adeno-acanthomata.
2 squamous cell.
2 anaplastic.

The average age of the menopause in these cases was 47 years, though in 2 cases associated with endometrial hyperplasia it was 53 years. One developed in a patient who had had a radium menopause 8 years previously. In another fibroid, cervical polypi and adenocarcinoma were all present—signifying the danger of accepting the obvious pathology as the only cause. In 3 cases carcinoma was associated with an active hyperplastic endometrium. Two cases were inoperable.

Other malignant cases were 3 cases (2.04 per cent) of squamous-cell carcinoma of vagina. One case of carcinoma of vulva. One case of carcinoma of ovary. One case of malignant granulosa cell with intravascular deposits.

Benign conditions accounted for 82 cases (55.8 per cent).

Twenty-nine cases (19.7 per cent) were ascribed to an oestrin effect on the endometrium. Seventeen showed an atrophic endometrium, 4 showed polypi. Four showed moderate oestrin stimulation and 2 showed hyperplasia. Two cases were due to indiscriminate use of stilboestrol.

Three cases occurred in patients who had had a radium menopause 2 to 6 years previously. The endometrium was atrophic.

Bleeding occurred after curettage in the 2 hyperplastic cases. Hysterectomy was done. The ovaries were atrophic. It is recognized (Novak, 1946) that post-menopausal active hyperplasia, in contradistinction to regressive hyperplasia which is the end result of anovular menstruation at the menopause, is a pre-cancerous condition. In at least 2 cases in this series all gradations were demonstrable between hyperplasia and adenocarcinoma.

In some cases the stimulation of the endometrium is due to an extraovarian source of oestrin

believed to be the adrenal cortex though it may be derived from chemical metabolites of the sterols.

The remaining causes discovered were:

Associated with prolapse, 13 cases (8.8 per cent). Senile vaginitis and endometritis, 12 cases (8.1 per cent). Cervical erosion, 7 cases (4.8 per cent). Urethral caruncle, 6 cases (4.08 per cent). Fibroids, 5 cases (3.4 per cent), 2 associated with carcinoma. Cervical polypi, 5 cases (3.4 per cent). Ulceration due to pessaries, 3 cases. Ovarian tumours, 3 cases. Extra-uterine causes, 2 cases, one due to gross anaemia following pyelonephritis and uraemia. One due to ? high blood-pressure.

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Mr. Stabler referred to a case reported in this series, who had been bleeding for 6 months and the menopause had been 20 years previously. Both ovaries were atrophic; therefore, he thought the oestrogen had been produced frof an extraovarian source.

Professor Jeffcoate congratulated Mr. Flett Smith on the presentation of his paper. He thought the most interesting point was hyperplasia in the presence of atrophic ovaries and the suggestion that it was due to the adrenals or the change of sterols. He thought we should be chary of accepting metropathia as due to the adrenals. In animal experiments he would not accept an extraovarian source even if the ovaries were atrophic—only if the ovaries had been totally removed. After removal of both ovaries bleeding from the uterus practically never occurs.

Professor Jeffcoate thought there were 2 types of metropathia (1) due to excess of oestrogen which is reversible and (2) due to a change in the endometrium which is irreversible.

Dr. S. B. Herd stressed the fact that a biopsy does not prove innocence and even curettage may not be enough. In 2 cases of his own 3 curettages were necessary before malignant disease was found. He thought malignant disease was present in more than 60 per cent of cases of post menopausal haemorrhage.

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Dr. Rutherford Morison said the modern curse is the indiscriminate use of synthetic oestrogens in post-menopausal cases.

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THE NEWCASTLE-UPON-TYNE OBSTETRIC EMERGENCY SERVICE.

Mr. Stabler said that the service was founded in 1935 and, until the end of 1936, 353 calls had been made and 8,356 miles travelled and 30 gallons of intravenous infusion given. The furthest distances travelled had been to Berwick 64 miles and Barnard Castle 41 miles. The population of the area was about 2½ millions. Subsidiary centres had been suggested. It was probably true that beyond 30 miles much of the value of the service was lost. But there were two necessities, the first was frequent use, the second was a suitable personnel. These two factors were more important than speed. The apparatus was always available for use by any practitioner; in fact it had never been called without a request for the attendance of a consultant. In the early days the object was to render a woman fit to stand the journey to hospital; 9 out of 27 women died, and this showed the danger of such a journey which was nowadays almost never necessary.

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motion, therefore a case was seldom reached in less than half an hour. The other limit was 2 hours to Berwick.

Experience showed that much of the mortality was due to deaths within a few minutes of the emergency arising. The women who survived half an hour could usually be saved within a reasonable time longer than this. Great care must be used in taking the address.

The conditions treated were 41 miscarriages (2 deaths), 20 antepartum (2 deaths), 45 intrapartum (6 deaths), 231 immediate postpartum (26 deaths), 15 late postpartum (2 deaths), and 1 not pregnant.

Mr. Stabler then gave details of each condition and its treatment. He discussed particularly the treatment of retained placenta.

Of the 37 deaths, 15 preceded the arrival of the squad. There remained 22 deaths in whom treatment was possible. These cases were analyzed. Many occurred in the days before there was adequate blood for transfusion.

Discussion.

Professor Claye congratulated Mr. Stabler on his excellent and timely review. It was generally agreed that the call should be to the hospital and not directly to a consultant.

A meeting of the Society was held in Liverpool, on Friday, 4th July, 1947.

The President, Professor A. M. Claye, was in the Chair.

Mr. Frank H. Edwards described a case of

ACUTE UTERINE INVERSION.

The patient was a primipara, aged 22. After a labour lasting 16½ hours she was delivered by low forceps of a 7 pounds 6 ounces infant. Despite good contractions the placenta had not separated 45 minutes later. Gentle rubbing of the uterus and mild pressure caused the placenta to present at the vulva. It was twisted out. Examination showed a ragged placenta and membranes. Ergometrine was given. The patient looked pale but the loss was normal. A depression in the fundus, thought to be due to a fibroid, was felt. The patient was then left and spent a restless night. In the morning her blood-pressure was 70/40, pulse 90, and she complained of pain in the pelvic region. The fundus was felt 2 inches below the umbilicus.

Two pints of plasma and one pint of blood were given. Her condition did not improve appreciably and another pint of plasma was given. There had been no undue loss, yet by evening her systolic blood-pressure was only 80.

Mr. Edwards was called to see her for the first time at 9.45 p.m. She had the appearance of suffering from extreme loss of blood. The uterus was 2 inches below the umbilicus and there was some abdominal rigidity. She was transferred to hospital and blood transfusion commenced. Her condition improved, but during the third pint she commenced to lose badly. Under anaesthesia a mass of clot, a strip of membrane, and a piece of placenta were removed from the vagina. A mass the size of a coconut was found in the vagina and bimanual examination revealed that it was the inverted uterus. The abdominal mass had now disappeared.

The uterus was replaced after about 10 minutes manipulation. The loss ceased immediately and the uterus resumed its normal shape. Another pint of blood and morphine were wiven. She made a good recovery. Penicillin and sulphadiazine were given prophylactically.

The speaker thought that the inversion was caused by a partial adherence of the placenta to the fundus, the free portion of the placenta acting as a polyp, being forced out by the uterus which then inverted itself.

He wondered why the uterus appeared to be so high in the abdomen.

Discussion.

Mr. Macintosh Marshall said that in his experience the inverted uterus may be high in the abdomen with the fundus in the vagina; it is inverted through the stretched lower segment. In this case he thought the inversion had been present from the beginning.

Mr. Scott Russell supported the statement that the uterus may be high in acute inversion.

Mr. F. J. Burke described

AN UNUSUAL CASE OF GRANULOSA-CELL TUMOUR.

In 1940 Mr. Burke was asked to give an opinion on a section of a tumour removed from the broad ligament. The histological appearances were quite unlike anything he had seen before. He thought it might be a teratoma.

Two and a half years later he saw a patient aged

42 years, married, with 3 children, and complaining of irregular uterine haemorrhage. In the late thirties she developed a large abdominal tumour which was removed by operation. For the next 2 years she had amenorrhoea followed by irregular slight bleeding.

Examination showed a large hard round fixed mass rising to the umbilicus and a midline scar. The cervix was healthy and the body of the uterus could be felt pushed over to the right.

Operation revealed a tumour with many adhesions occupying the left broad ligament and retro-peritoneal tissues. It was firmly united to the uterus. The right ovary was normal, the left could not be found. The tumour was removed along with the uterus and its appendages, laying bare a large area of the pelvis and posterior abdominal wall which could not be covered with peritoneum. The patient did well for several days, then developed paralytic ileus and died on the eleventh day.

Postmortem examination failed to show evidence of any secondary growth in the thorax or abdomen.

Macroscopic examination showed a large, encapsulated, smooth tumour. The cut surface was greyish white and showed fine lobulation. It contained a few small cysts and there were haemorrhagic areas. The uterus was grossly hypertrophied, with a relatively thin endometrium. The round ligaments were very thick.

Microscopic examination showed the exact histological appearance of the slide the speaker had been unable to classify in 1940. The records showed that both tumours had been removed from the same patient. Different areas of the second tumour showed different appearances. In some areas there was a superficial appearance of thyroid tissue, and in others of testicular tissue.

In conclusion, Mr. Burke said that several pathologists had seen the sections. Granulosa-cell tumour had been suggested, mainly on the rosette appearance, which was seen in tumours other than granulosa cell, such as basal-cell carcinoma, salivary adenoma, some malignant mammary tumours and particularly in neuroepithelioma of the retina. A teratoma of nerve tissue, and a well differentiated arrhenoblastoma, although the patient showed no evidence of maleness, had also been suggested. Weighing all the evidence it seemed probable that it was an atypical granulosa-cell tumour with malignant characteristics.

Discussion.

Professor Jeffcoate said the rosette and palisade appearance were typical of granulosa-cell tumours and of arrhenoblastoma, but the clinical picture supported the granulosa-cell theory.

As a contrast Dr. Walsh showed a specimen from a typical case of granulosa-cell tumour.

Mr. F. J. Burke reported a case of

COMPLETE TORSION OF A FIBROID UTERUS.

Mr. Burke said that torsion of the uterus was rare. Most cases had occurred in Europe. Only 8 cases had been recorded in the American literature.

The patient, a spinster aged 74 years, had been seized with severe abdominal pain and vomiting while at breakfast. At noon her doctor gave her ¼ grain morphine. She had had 2 similar but less severe attacks 10 days, and 6 months previously.

Mr. Burke saw her at 2.30 p.m. She was a small emaciated woman suffering from severe shock. A large hard tumour was felt rising to above the umbilicus. There was little or no rigidity. The tumour could not be reached by rectal examination nor could the cervix be felt. Torsion of a fibroid was diagnosed.

After intravenous saline and a second injection of morphine her condition improved and operation was performed under local analgesia at 7 p.m. A plum-coloured tumour and blood-stained peritineal fluid were found. The tumour was attached by a pedicle rising from the centre of the pelvis, pink and vascular at its lower attachment and black where it merged into the tumour. It was no thicker than an index finger. The pedicle was divided and the tumour removed. The cut surface was obviously the cervix with blood vessels on either side of it. The patient made an excellent recovery.

Examination of the specimen revealed a uterus with both appendages and multiple fibroids. The uterine cavity was 6 to 7 inches in length and the lowest part was thinned out cervix about one inch in length. Torsion had occurred at the level of the supravaginal cervix and was through more than 360 degrees.

The speaker said that about 170 cases of torsion of the uterus had been recorded, and might be classified as follows:

(a) Of the pregnant uterus with fibroids and without fibroids.

(b) Of the non-pregnant fibroid uterus. These may be divided into primary torsion where the tumour was sessile and secondary when torsion of the body was secondary to torsion of a pedunculated sub-serous fibroid.

In one series of 39 cases the tumours were sessile in 35. Almost invariably the sessile tumours produce asymmetry of the uterus, and this was considered to be an important predisposing factor. Pedunculated tumours were less likely to cause torsion and tend to do so when the attachment to the uterus was at or near the mid-line. It had been generally agreed that an irregular body movement such as turning over in bed initiated acute torsion which was maintained by spasm of the abdominal muscles. Repeated alterations in the shape of adjacent organs may promote less acute torsion. Vautrin had made out a strong case for repeated filling and emptying of the left sacral fossa. He maintained that this was the explanation of the normal dextrorotation in pregnancy.

More important was the anatomical derangement produced by the tumour. Backward and forward movements of the body of the uterus were unrestricted but axial torsion above the cervix was normally prevented by the broad and round ligaments. In many cases the patient was old, the tumour large, and senile atrophy of the ligaments had occurred, because the main tumour mass remained above the pelvic brim, and the cervix and broad ligaments became elongated and formed a thin pedicle. This undoubtedly was the explanation of torsion in the present case.

In most cases the site of torsion was the isthmus because Mackenrodt's ligament and the vaginal ligaments are well able to withstand rotational strain. In very few torsion had occurred in the body.

The degree of torsion was variable, on the average about 180°. Cases have been reported of torsion through 2 or more full turns of the pedicle.

The correct diagnosis was usually not made. There was nothing to indicate that the uterus was the affected organ. The severity of the symptoms was not proportionate to the size of the uterus or the degree of torsion. Bastianelli recorded a case in which spontaneous amputation occurred at the level of the cervix but gave rise to comparatively mild symptoms.

The results of operative treatment were surprisingly good. The mortality for treated cases was 11.1 per cent and for untreated cases 75 per cent. Subtotal hysterectomy was usually done, but if the tissues were viable and the patient was young myomectomy might be sufficient. Freund had reported a case in a patient 21 years of age. Mr. Burke said that so far as he was aware his case was the oldest on record. He thought that effective pre-operative treatment for shock and local anaesthesia had been important in achieving a successful outcome.

Discussion.

Mr. Scott Russell said he had seen one case in a woman after the menopause. He thought the significant diagnostic points were midline pain and vomiting more severe and persistent than in torsion of ovarian cysts or pedunculated fibroids.

In reply Mr. Burke said that from what he had read it was not easy to be dogmatic about symptoms of torsion. Small tumours might have big signs. In torsion of the uterus there was usually a history of preceding attacks.

Professor Jeffcoate read two short papers.

1. CORRECTION OF THE POSITION OF THE UTERUS BY THE USE OF A HODGE PESSARY, and

2. PYREXIA AS A SIGN OF ENDOMETRIOSIS.

These will be published in a later issue of the JOURNAL.

Mr. Harvey Evers read a paper on

AN INTERESTING CASE OF HAEMATOMETRA.

The patient, aged 50 and nulliparous, had been married for 22 years. She complained of irregular bleeding for 4 years culminating in 4 irregular losses in 5 weeks. There had been no pain.

Examination showed a slight symmetrical enlargement of the uterus. The cervix was nulliparous, and the vulva, vagina, and uterine appendages normal.

Dilatation and curettage showed a uterine cavity 4 inches in length, myometrial hypoplasia, and scanty microscopically normal curettings. Fifty mg. of radium were inserted for 48 hours. Two weeks after discharge from hospital she had a normal period. Twenty-eight days later she had another painless period lasting 2 days. This was followed by a slight irregular blood-stained loss.

Examination revealed a uterus not diminished in size despite the lapse of 3 months. For the next 9 months she had no more bleeding and remained perfectly comfortable. Then she began to have attacks of lower midline abdominal pain, which increased in number and severity for 4 months. The attacks lasted 4 to 5 hours at about 5-day intervals.

Examination showed that the uterus had increased in size and again 3 months later it had almost doubled its size. The pain had become much worse.

An attempt was made to dilate the cervix but the internal os could not be found. Therefore laparatomy was performed and the uterus, tubes, and ovaries removed.

The uterus was the size of a 4 months' pregnancy, the Fallopian tubes oedematous and the ovaries atrophic. The uterus contained thick black fluid. No communication between the cervix and vagina could be detected.

Microscopical examination showed:

(1) Extremely atrophic endometrium with sub-epithelial dilatation and congestion of vessels.

(2) Diffuse adenomyosis of myometrium.

(3) Some blood clot in the lumen of the Fallopian tubes and evidences of subacute salpingitis.

(4) Ovary showed a single cell layer of germinal epithelium with no ova and no primordial follicles. Cortical stroma of theca type rather prominent.

Discussion.

Mr. Burke mentioned a case where radium had been used for a patient with cervical erosion who became pregnant and delivered normally but a severe cervical laceration had to be sutured. She did not menstruate again. Two years later she complained of dysmenorrhoea. The uterus was not enlarged. She was found to have endometriosis due to retrograde menstruation.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts and titles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.I. There is special need of abstracters in foreign languages and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

INDEX

ANATOMY

572. A Method of Radiopelvimetry of the Pelvic Inlet. (Une méthode de radio-pelvimétrie du détroit supérieur.)

By P. ROSA. *Gynaecologia, Basel,* **123,** 137–166, Mar. 1947. 14 figs., 5 refs.

An accurate method (an elaboration of Von Schubert's method) is described for the determination of the true conjugate diameter of the pelvic inlet and of the inclination of the plane of the inlet to the vertical. Both can be determined from a lateral radiograph of the pelvis taken with the patient in the upright position. Before radiography a graduated notched metallic ruler is inserted between the thighs of the patient as high as it will go and accurately placed in the sagittal plane of the patient The patient is then placed in the Albert semi-sitting position. As the inclination of the pelvic brim to the vertical is known from the lateral view, the pelvic brim can be so adjusted as to make it exactly parallel to the plane of the film. A notched metallic ruler is placed in the plane of the brim and a radiograph of the brim and ruler is obtained. On this radiograph all the other diameters of the pelvic brim can be read. The author claims an accuracy up to 2 mm. for this method.   *A. Orley*

573. Use of a Lateral Radiograph of the Sacrum in Obstetrics. (De l'utilité de la radiographie du sacrum de profil en obstétrique.)

By P. TRILLAT, R. BURTHIAULT, and J. GONNET. *Gynéc. Obstét.,* **45,** 434–437, 1946. 6 figs., 25 refs.

At the Hôtel-Dieu, Lyons, 80 lateral radiographs of the sacrum in pregnant women have been taken since 1942. These are classified into six groups with reference to the appearance of the anterior surface of the sacrum: (1) Normal. The curve of the sacrum is maintained and the lumbo-sacral angle (between the anterior surfaces of L5 and S1) is 110 degrees. The promontory is found to be more commonly formed by the upper lip of the first piece of the sacrum than by the lower lip of the last lumbar body. (2) The sacrum with an exaggerated concavity. The promontory is well-marked and formed by S1, and the lumbo-sacral angle is 90 to 100 degrees. The lower end of the sacrum is sometimes hooked sharply forward. (3) The straight sacrum, the concavity of which has disappeared. The lumbo-sacral angle is nearly 180 degrees. (4) The intermediate sacrum, whose curve is straightened out superiorly opposite the first piece, so that the lumbo-sacral angle again approaches 180 degrees, while the lower part of the sacrum is sharply curved. Thus a false promontory exists opposite the junction of S1 and S2. (5) The sacrum with a normal concavity but a very obtuse lumbo-sacral angle approaching 180 degrees. (6)

Atypical forms, such as those with sacralization of the last lumbar vertebra.

S. S. B. Gilder

PHYSIOLOGY

574. Hydrogen Ion Concentration (pH) of Normal Vaginas.

By J. KARNAKY. *West. J. Surg.,* **55,** 103–106, Feb. 1947. 21 refs.

The history of the study of vaginal acidity is outlined, and a survey of the methods of determination given. The author used the Beckman pH meter and Rakoff's vaginal electrodes to study vaginal pH in 52 pregnant and 15 non-pregnant women. This report differs from previous ones in that the author has determined the pH in different sites of the vagina—namely, anterior fornix, posterior fornix, and left and right lateral walls, the averages for these being 4.26, 4.37, 4.34, and 4.46 respectively. In non-pregnant women the average was 4.34, while in pregnancy the figure was 4.38. The overall pH average in apparently normal vaginas varies between 3.27 and 4.99.

C. W. Kimbell

575. Vaginal Smears. (Les frottis vaginaux.)

By A. LICHTWITZ and M. FITOUSSI. *Sem. Hôp. Paris,* **23,** 687–708, Mar. 21, 1947. 2 synoptic tables, 24 figs., 78 refs.

[This well-written and important article is subdivided into four parts. It is well worth reading in the original, especially the adequately illustrated part dealing with the description of the cells found in vaginal smears in the various stages of the menstrual cycle.]

576. Vaginal Smears and Other Methods of Ovarian Examination. (Les frottis vaginaux et les autres methodes d'exploration ovarienne.)

By A. LICHTWITZ and M. FITOUSSI. *Sem. Hôp. Paris,* **23,** 687–688, Mar. 21, 1947.

The exact estimation of ovarian function is very difficult because of the multiple and complex hormonal interrelations between the ovaries, the pituitary body, the suprarenal cortex, and the thyroid gland. Although the pituitary controls ovarian secretion, it can be inhibited itself by excessive ovarian hyperactivity and by extraneous nervous influences (especially those arising from the infundibulum), as well as by external factors such as inadequate diet and more especially lack of proteins. The suprarenal cortex is concerned not only with the production of oestrone, progesterone, and androgens, but also with water and salt metabolism and the vegetative nervous system. The thyroid-ovarian interrelations are equally complicated. Normally ovarian secretion appears to occur in a fixed cyclical manner: (1) no secretion during menstruation to allow secretion of the follicle-stimulating hormone by the pituitary; (2)

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moderate secretion of folliculin after cessation of menstrual flow to prevent too early ovulation; (3) progressively increased amount of folliculin producing ovulation round about the 14th day; (4) secretion of progesterone after ovulation has occurred, and change in the character of the oestrogen secreted (probably oestradiol and oestrone before ovulation and oestriol after ovulation); (5) finally diminution of the amount of folliculin secreted, leading to spasm and then dilatation of the mucosal spiral arteries, this in turn resulting in submucosal haemorrhages, necrosis, and menstruation. It is thus evident that it is very difficult to identify clinically the various processes producing symptoms of ovarian dysfunction.

Nicolas Tereshchenko.

577. **Vaginal Smears. Technique of Obtaining Samples, Staining, and Interpretation of Results.** (Technique des prélèvements, coloration, et interprétation des résultats.)

By A. Lichtwitz and M. Fitoussi. *Sem. Hôp. Paris*, **23**, 688–695, Mar. 21, 1947. 15 figs., 30 refs.

The technique of obtaining and examining vaginal smears is simple, can be repeated as often as necessary (even daily), and appears to give reliable information. Papanicolaou first demonstrated the presence of changes in the vaginal mucosa of guinea-pigs in 1917. In 1933 he showed that similar changes occur in the vaginal epithelium of women. The samples are obtained by means of a glass pipette to which a rubber bulb is fixed. It is important that the vagina should not be swabbed or otherwise cleansed before the sample is obtained, nor should a sample be taken within 12 hours of intercourse. The contents of the posterior third of the vagina are aspirated, the pipette being inserted in several different directions. The material obtained is ejected on to a slide and immediately, while still wet, fixed by means of a solution of equal parts of 95 per cent alcohol and ether (most conveniently by plunging the slide into a wide-mouthed jar containing the fixing solution). The specimen must remain in the solution until it is stained with haematoxylin and eosin; it is then cleared and mounted in Canada balsam. Five types of cells, and their modifications, are found in vaginal smears; in addition, leucocytes, erythrocytes (which should be washed off the slide by immersion for 5 minutes, after fixing, in a 10 per cent solution of acetic acid of smears obtained during menstruation), organisms, and mucus are often present. The cells are: (1) Small, round or oval, basophil cells, with a large nucleus containing distinct chromatin granules, a few vacuoles being seen in the cytoplasm. These are normally present before puberty or after the menopause; outside these periods of life their presence indicates atrophy of the vaginal mucosa due to lack of oestrogenic activity; these cells may also be found postpartum or in infections of the cervix, but they show in that case more variation in size, more pronounced vacuoles, irregularly-shaped nuclei, and sometimes faint eosinophilia. (2) A larger, less strongly basophil cell, with a slightly smaller nucleus, still containing distinct granules; this is the cell most frequently seen. (3) Elongated (navicular) boat-shaped cells, with an often eccentric and indented nucleus, the cytoplasm being unusually condensed at the periphery with perinuclear vacuolation; usually these are only seen during the week following cessation of the menstrual flow and indicate limited oestrogenic activity; a modification of these cells is seen during pregnancy. (4) Large, polygonal, keratinized, still basophil cells, with a small pyknotic nucleus; they indicate moderate oestrogenic activity. (5) Large, polygonal, keratinized, eosinophil cells with a small nucleus (which may occasionally be absent); they indicate normal maximal oestrogenic activity. The last two types of cell are modified after ovulation: they become creased, their edges curl, and they are then called regression cells; these changes indicate either the presence of lutein or a diminution in the amount of folliculin. In addition the following points may be noted: the cells are usually grouped together before ovulation and in the pre-menstrual phase, while during ovulation they remain separate; mucus is rare just before and during ovulation but abundant in the premenstrual and postmenstrual phases; leucocytosis is an indication of infection or of poor oestrogenic activity. The amount of glycogen present in the cells (estimated by the depth of staining with iodine vapour) is a measure of oestrogenic activity and increases as the *p*H diminishes. A detailed account of the normal appearances during the various phases of the normal menstrual cycle is given, and is best summarized in the following table:

Phase:	Menstruation			Post-men-strual	Pre-ovular	Ovula-tion	Post-ovular	Pre-men-strual
Day of cycle:	1st	2nd	5th	5th–9th	10th–12th	13th or 14th	15th–18th	19th–last
Keratinized cells:	20%	40%	20%	10%	50%	60%	35% (Regression cells)	5%
Basophil cells with small nuclei:	50%	25%	50%	70% (including navicular cells)	40%	30%	40%	75%
Basophil cells with large nuclei:	30%	35%	30%	20%	10%	10%	25%	20%
Leucocytes:	Very numerous			Numerous	Scanty	None	Numerous	
Mucus:	Abundant				Scanty	None	Abundant	
Erythrocytes:	Numerous			None		Scanty	None	

Nicolas Tereshchenko

578. Influence of X-rays on the Gonadotrophic Function of the Pituitary Gland. (Uber den Einfluss der Röntgenbestrahlung auf die gonadotrope Funktion der Hypophyse.)

By A. BAIDINS, L. CLAESSON, and A. WESTMAN. *Gynaecologia*, 122, 347–362, Dec. 1946. 30 refs.

The effect of X-rays on the function of the pituitary gland in the rat was investigated by some careful systemic experiments. Literature on the effect of X-rays on the pituitary gland is profuse; clinical workers have used X-rays therapeutically with varying results. There is much less literature on the effect of X-rays in animals, and again results differ. It is agreed that small doses produce no histological changes, but there are varying reports of secondary effects on other glands. The difference in results may be due to variations in technique and dosage or other factors, but most papers are not sufficiently clear to assess these factors.

In the authors' experiments 61 immature female white rats were used, 38 for the experiment and 23 for control; all were under comparable conditions. A dosage of from 2 to 12,000 r was given, the dosage being measured by a physicist. The rat was covered with radio-opaque substance except for a small window during treatment to avoid other effects. A daily vaginal smear was taken and the rat weighed every 3 days. Observation continued up to 15 weeks, and after death the pituitary gland and ovaries were weighed and measured and sections including serial sections taken. The rats were divided into 3 groups, group 1 receiving from 2 to 45 r, group 2 from 50 to 1,000 r, and group 3 from 6,000 to 12,000 r. The first 2 groups tolerated the irradiation well and there was progressive increase in weight.

In group 1, which was subdivided into 3 groups according to the duration of observation, increase in weight was the same as in the controls; the time of onset of oestrus varied but occurred frequently before the sixth week: similar variations, however, occurred in the controls. The findings were similar in group 2 and the ovarian cycle was normal. In group 3 all the rats became rapidly ill and died. In group 1 both the pituitary gland and the ovaries were larger and weighed more than in the controls; in group 2 the pituitary weighed more but the ovaries were smaller and weighed less; while in group 3 both the pituitary and the ovaries were smaller and weighed less. Microscopically, there was hyperaemia of the pituitary gland and the ovaries in group 1, but no cell changes were observed. In group 2 there was hyperaemia of the pituitary gland and in 1 case a reduction of the eosinophil cells and a small effusion of blood. In group 3 there was marked necrosis of the gland but fixation had been delayed some hours.

The authors conclude that with doses from 2 to 1,000 r to the pituitary gland there were no certain changes in function of the gland or other glands. That there was an effect was shown by the increase in weight and size of the gland, but the only microscopical change was hyperaemia. No functional change in the ovaries was observed. These results differ from those of most other workers. However, a pathological pituitary gland may be influenced by X-ray doses which have no effect on a normal gland.

L. W. Lauste

579. The Speed of Appearance of Glycogenic Vacuoles in the Ovariectomized Woman (Treated with Folliculin) after Progesterone Administration. (De la vitesse d'apparition des vacuoles glycogéniques chez la femme ovariectomisée, folliculinisée, lors de la charge progestinique.)

By J. FERIN. *Ann. d'Endocrinol.*, 8, 69–75, 1947. 5 figs., 8 refs.

Although small quantities of glycogen granules are demonstrable in the endometrium during the folliculin phase of the menstrual cycle, the presence of massive amounts of glycogen, as shown by the appearance of basal vacuoles in the glandular epithelial cells, is diagnostic of the lutein phase. The author has used this fact to determine the speed with which an injection of progesterone would produce an effect on the endometrium in 3 ovariectomized women to whom folliculin had previously been given. After a single dose of 30 mg. given intramuscularly basal vacuole formation was seen within 24 hours, the time of appearance varying from one subject to another. Glycogen was found first as fine granules in the superficial epithelium and in the necks of the glands. Within a few hours granules were also found in the depth of the glands.

S. S. B. Gilder

580. Comparative Efficacy of the Perlingual and Gastro-intestinal Routes in the Administration of Anhydro-oxyprogesterone to an Ovariectomized Woman. (Efficacité comparée des voies d'administration perlinguale et gastro-intestinale de l'anhydro-oxyprogestérone chez une femme ovariectomisée.)

By J. FERIN. *Ann. d'Endocrinol.*, 8, 62–65, 1947. 1 fig., 9 refs.

Experiments were made with varying amounts of anhydro-oxyprogesterone given by the perlingual or gastro-intestinal route to an ovariectomized woman previously treated for several months with oestrogens and progesterone. The presence of large basal glycogenic vacuoles in the gland cells of the endometrium was taken as an indication of a luteinizing effect. No advantage of the perlingual route over the gastro-intestinal one was seen. The daily threshold-dose of the hormone required to produce an effect capable of histological demonstration was 15 mg. by either route. A study to determine for each oestrogen, administered by various routes, the minimal quantity required to produce a histologically demonstrable effect is advo-

cated. The author proposes to call this quantity the " woman-unit " of oestrogen.

<div align="right">S. S. B. Gilder</div>

581. The Formation Mechanism of Oestrogenic Hormones. I. The Presence of an Oestrogen-precursor in the Rabbit Ovary. [In English.]

By L. CLAESSON and N. HILLARP. *Acta. physiol. scand.*, **13**, 115-129, Feb. 15, 1947. 4 figs., 18 refs.

The authors have demonstrated the presence of a birefringent substance in the theca interna and interstitial tissue of the rabbit ovary, which from its reaction to histochemical reagents and lipid solvents appears to be a sterol of the cholesterol type. A relation was established between the presence of birefringent substance and cholesterol content which indicates that the birefringent is probably due to cholesterol. The material is present in large amounts in the ovaries of oestrous, pregnant, and pseudo-pregnant females, but almost absent from the ovaries of immature and anoestrous animals. Strong gonadotrophic stimulation reduces the ovarian content of the substance. The parallelism between oestrogenic activity and the ovarian content of the sterol suggests that it is a precursor of oestrogenic hormones.   E. F. McCarthy

582. The Normal Menstrual Cycle. (El ciclo menstrual normal.)

By A. ALVAREZ BRAVO. *Rev. méd. Hosp. gen.*, **9**, 421-433, Mar. 1947. 8 figs., 42 refs.

583. Lutein Function in Tuberculous Female Patients, Demonstrated by a Study of the Temperature Chart. (La fonction lutéinique de la femme atteinte de tuberculose pulmonaire, appréciée par l'etude de la courbe thermique.)

By A. LAFONTAINE, J. FERIN, and J. PIRE. *Ann. d'Endocrinol.*, **8**, 53-56, 1947. 1 ref.

The temperature charts of 276 women under treatment in a sanatorium for active pulmonary tuberculosis were studied. All the patients were menstruating normally and the study was prolonged over at least four menstrual cycles. Four types of curve were seen : premenstrual rise in temperature (90 per cent); premenstrual and menstrual rise (8 per cent); menstrual rise (1 per cent); fall in the ovulatory part of the cycle, sometimes followed by a menstrual rise (1 per cent). In the majority of cases the physiological rise in temperature during the lutein phase of the cycle superimposed itself accurately on the diurnal variations due to the pulmonary tuberculosis, the type of curve being constant for each individual. Where menstrual cycles were unduly prolonged the rise in temperature due to the action of lutein was also prolonged. An increase in the erythrocyte sedimentation rate occurred in 80 per cent of cases during menstruation but did not run parallel to the premenstrual rise in temperature. Administration of testosterone propionate, 3 doses of 25 m.g., had

an inhibiting effect on the premenstrual rise in temperature in 12 out of 48 cases.

<div align="right">S. S. B. Gilder</div>

584. Functional Uterine Haemorrhage. (Hémorragies utérines fonctionelles.)

By P. MEUNIER. *J. Hôtel-Dieu, Montreal*, **15**, 26-45, Jan.-Feb., 1947. 18 refs.

585. Effect of Cardiazol Shock on Ovulation in the Rabbit. (Der Einflus des Cardiazolschoks auf die Ovulation beim Kaninchen.)

By K. RICHTER. *Wien. med. Wschr.*, **97**, 153-155, Mar. 29, 1947. 5 figs., 10 refs.

" Cardiazol " (leptazol), 12 to 20 mg. per kilo, was injected intravenously into rabbits, the ovaries of which had been inspected at a preliminary operation. In 1 animal so treated no ovulation occurred. In 5 other animals 6 similar injections were carried out with 6 days, and here in " about 50 per cent of the cases " ovulation was observed. It is suggested that the cardiazol shock induces ovulation through nervous pathways.

<div align="right">H. Herxheimer</div>

586. The Time of Ovulation in Shortened Menstrual Cycles. (Zur Frage des Ovulationstermins beim verkürzten Zyklus.)

By H. KRETSCHMAR. *Zbl. Gynäk.*, **69**, 283-285, 1947. 1 fig.

587. Abortive Ova. II. An Investigation into the Abnormal Appearances of the Chromosomes in Mammals during Maturation. (Uber Abortiveier. II. Untersuchungen uber die in Chromosomensatz der Säugetiereizelle während der Reifeteilunger sich abspielenden abnormen Erscheinungen.)

By P. VARA and S. PESONEN. *Acta. obstet. gynec. scand.*, **27**, 215-248, 1947. 29 figs., 25 refs.

588. An Experimental Study of the Influence of Haemorrhagic Anaemia on the Ovarian Function. [In English.]

By G. SUNDELIN. *Acta. physiol. scand.*, Suppl. **40**, 1-52, 1946. 5 figs., bibliography.

The author produced an experimental anaemia in rats by cutting off their tails and immersing the stumps in hot water to make them bleed, his object being to study the effect of the anemia on ovarian function. In 68 of the 69 animals the ovarian cycle was suspended for varying periods of time. The rat at this time accepted coitus but did not become pregnant or pseudo-pregnant. The changes were, however, reversible, and the cycle became normal again when the anaemia was cured. The vital factor in the loss of the ovarian function seemed to be the loss of red blood cells and haemoglobin or of the iron. In 7 out of 8 rats it was possible to prevent the change in the ovarian cycle by injection of iron and ammonium citrate. During the anaemia the ovary lost about a third of its normal

weight, but there were no apparent histological changes as compared with normal ovaries.

F. J. Browne

589. **Contractile Activity of the Uterus and Vitamin B$_1$.**
By V. M. Chernov, P. N. Mazaev, and N. A. Kudryavina. *Akush. Ginek.*, 1, 16–20, 1947. 3 figs., 1 ref.

During an investigation of the pharmacological properties of the vitamins it was observed that vitamin B$_1$ (thiamine or aneurine) appeared to have an action similar to that of acetylcholine. Stimulation of the cut vagus nerve has actually produced thiamine as well as acetylcholine. The authors have conducted two series of experiments on the action of vitamin B$_1$ on uterine muscle. In the first series three small lead beads were implanted into the broad ligament of non-pregnant female rabbits alongside one of the uterine horns. About 7 to 9 days later a series of radiographs were taken before and after the administration of vitamin B$_1$; the distance between the beads was carefully measured and taken as an indication of the degree of contraction or relaxation of the uterine muscle. All the pictures were taken with an exposure of 0.1 sec., a focal distance of 60 cm., and a power of 45 kW. and 40 mA. Thiamine was given intravenously in doses of 0.5 mg., 1 mg., 6 mg., and 60 mg., and pictures were taken 30 seconds, 1 minute, 2 minutes, 5 minutes, and 10 minutes after the injection. There was a definite effect on the uterine muscle, 25 to 50 per cent of shortening being obtained with doses of 1 mg. or more (no effect was demonstrable with 0.5 mg. of thiamine). In the second series the rabbits and some guinea-pigs were killed, and a uterine horn placed in a glass container of a capacity of 70 ml. To the container 17.5 mg. or 30 mg. of vitamin B$_1$ was added, and the resulting contraction recorded. In all experiments pronounced increase in tonus and an increase in the amplitude of the rhythmical uterine contractions occurred almost immediately, and lasted for about 25 minutes. The authors conclude that vitamin B$_1$ is an important uterine stimulant.

Nicolas Tereshchenko

590. **Pharmacology of β-glycerophosphate of Sodium. Spasmolytic Effect on the Uterus. Analeptic Effect on the Respiratory Centres.** (Farmacología del β-glicerofosfato sódico. Acción uteroespasmolítica. Acción analéptica respiratoria.)
By B. Lorenzo Velazquez, P. Garcia de Jalon, and R. Perez Carnicero. *Obstet. ginec lat.-amer.*, 4, 827–835, Nov. 30, 1946. 5 figs., 7 refs.

The action of glycerin on smooth muscle is discussed, and the authors then report their experimental findings with the glycerophosphates. The β-glycerophosphates were found to be more effective than the α-glycerophosphates, and the magnesium salt was more effective than the sodium one. The

following conclusions are drawn; (1) With relatively weak concentrations of sodium β-glycerophosphate (between 1 in 100 and 1 in 1,000) in *in vitro* experiments the normal contractions of the uterine muscle of rabbits and guinea-pigs are diminished but not abolished. (2) The same concentrations used after spasm has been produced by histamine, ergotamine, pituitrin, and pilocarpine cause a rapid relaxation, but the later response to the same dose is diminished. (3) An injection of 3 ml. of 25 per cent solution given *in vivo* causes a complete relaxation of the uterus after the administration of ergotamine. (4) In animals suffering from a deficiency of vitamin B$_1$ the response is negative or only slight. The drug also fails to act in cases of polyneuritis and hypovitaminosis in pregnancy. (5) Repeated doses produce a summation of effects, but the drug has been found to have only slight toxicity in both experimental and clinical work, and this has been confirmed by other workers. (6) In experimental animals whose respiratory centre had been depressed by drugs, sodium β-glycerophosphate was found to have a marked analeptic action; favourable results have been reported in the treatment of asphyxia in the newborn.

Bryan Williams

591. **Pharmacological Effect of Uterine Oxytocics and Sedatives on the Fallopian Tube.** (Acción farmacológica de occitócicos y sedantes uterinos sobre trompa. Contribución a la farmacología de la trompa.)
By M. Roncalès Cativiela. *Farmacoter. actual*, 4, 26–29, Jan. 1947. 5 figs.

The pharmacology of the Fallopian tubes has been little studied and there is dispute about the respective parts played by the ciliary and peristaltic actions of the tube in the passage of the ovum. In the rabbit transformation of the ciliary cells into secretory cells takes place under the influence of the ovarian hormones, and there is evidence that in the human being a similar change takes place in the uterine part of the tube. Almost all investigators agree that the strength and uniformity of the cilia diminish towards the uterus as the lumen of the tube decreases. Readings taken at insufflation show that there are 3 or 4 regular oscillations of pressure a minute of 10 to 15 mm. extent. These are due to peristaltic action and are not observed when the tubes are blocked. In view of the time taken for the transit of the ovum it does not seem likely that peristalsis is the only factor. Further, the tube does not respond to direct stimulation like the ureter. According to Grosser the ovum reaches the isthmic part of the tube fairly quickly by ciliary action and lies there in a sulcus, where it produces a slow but progressive irritation of the muscle, which eventually causes it to be moved into the uterus by peristaltic action.

In a preliminary report the author describes in detail his experimental methods. The tube is re-

moved with a minimum of trauma and used as soon as possible. Longitudinal strips of about 2 cm. length are placed in a bath under carefully controlled conditions and are used in making tracings. The normal spontaneous movements show a rapid contraction with slow relaxation interrupted by a secondary wave of contraction. " Ginergino " produces a slight increase of the amplitude of contraction with slowing and the disappearance of the secondary wave. Ergometrine in adequate dose increases the contraction. " Doryl " (carbachol) has some paralysing effect. Sodium β-glycerophosphate has a sedative and finally a paralysing action. The author concludes that the response of the tube to drugs is not identiical with that of the uterus, and of the drugs hitherto used only ergometrine has a stimulating effect; sodium β-glycerophosphate has a sedative effect similar to its action on the uterus.

Bryan Williams

592. Some Preliminary Experiments in Connexion with the Effect of Prostaglandin on the Uterus and Tubae *in Vivo*. [In English.]

By J. ASPLUND. *Acta. physiol. scand.*, 13, 109-114, Feb. 15, 1947. 2 figs., 12 refs.

The effect of sperm plasma and prostaglandin was investigated *in vivo* on parts of the reproductive organs of the female rabbit. Intravenous or intraperitoneal administration of prostaglandin caused an increase in uterine tone and amplitude of contraction concurrently with the circulatory depressor effect. Evidence was obtained that prostaglandin, or at least a depressor fraction of this substance, is absorbed from the uterus and vagina. Sperm plasma and prostaglandin diminish the tonus of the abdominal Fallopian-tube ostium. It is suggested that these properties of sperm plasma facilitate the transport of spermatozoa.

E. F. McCarthy

PREGNANCY

593. Proteinaemia in Normal and Pathological Pregnancy. (La protidemia en el embarazo normal y pathológico. Con estudio especial de las diversas fracciones globulinicas.)

By J. LEON and B. BRAIER. *Obstet. Ginec. lat.-amer.*, 4, 809-825, Nov. 30, 1946. 2 figs., 61 refs.

After reviewing the literature on the blood proteins and their various fractions in normal and toxaemic pregnancy, the authors report fully and with detailed tables their findings in 11 cases of normal pregnancy and in 12 of toxaemic pregnancy, in some of which repeated examinations were made. The methods of Kjeldahl and Howe were used, and a special study was made of the globulin fractions (euglobulin, pseudoglobulin I, and pseudoglobulin II). In normal pregnancy they confirmed the fall

in total protein which has been found by other authors, but their results show an absolute and relative fall in albumin and a rise in globulin. The figure for the albumin-globin ratio was found to be 1.94, compared with one of 2.4 for healthy non-pregnant females. The euglobulin remained normal with a slight increase in pseudoglobulin II. In glomerulonephritis of pregnancy there was a slight decrease of total protein compared with normal pregnancy, with a big decrease of albumin and a big increase of total globulin. The albumin-globulin ratio fell to 1.7. Euglobulin was normal, with a slight increase of pseudoglobulin II. In pre-eclampsia and eclampsia there was a marked decrease of total proteins. The relative decrease of albumin was equal to that found in normal pregnancy, but the absolute decrease was greater. The globulins were increased in the same proportion as in normal pregnancy. There were no changes in pseudoglobulins I and II, but the euglobulin was *increased both absolutely and relatively to twice* the levels found in non-pregnant patients and in cases of normal pregnancy. In 9 cases in which euglobulin estimations were made they were found to average 21 per cent of the total globulins of the serum, instead of the normal 8 to 10 per cent. Before more definite conclusions can be drawn the authors consider that more estimations should be made in both normal and abnormal patients, preferably before and during pregnancy and after delivery.

Bryan Williams

594. Effect of Oestrogens on the Uterus during Early Pregnancy. (Au sujet de l'action des oestrogens sur l'utérus gravide des premiers mois chez la femme.)

By P. BADER. *Gynéc. Obstét.*, 46, 56-61, 1947, 25 refs.

595. Circulatory Anastomosis of Dizygotic Placentas. (Sobre las anastomosis circulatorias de las placentas dizigóticas.)

By M. L. PÉREZ, J. R. FIRPO, and E. M. BALDI. *Obstet. Ginec. lat.-amer.*, 5, 5-22, Jan.-Feb., 1947. 11 figs., 14 refs.

596. Estimation of Tocopherol (Vitamin E) in the Blood Serum and Milk and the Tocopherol Content of the Blood Serum, especially during Pregnancy and Lactation. [Sur le dosage du tocophérol (vitamin E) dans le sérum sanguin et le lait, et sur la teneur du sérum en tocophérol particulièrement pendant la grossesse et la période de l'allaitement.]

By L. RAURAMO. *Acta obstet. gynec. scand.*, 27, Suppl. 2, 1-77, 1946. 2 figs., Bibliography.

597. Use of Specific Gravity Method for the Determination of Haemoglobin, Haematocrit Value and Blood Proteins in Obstetrics and Gynaecology. (L'impiego del metodo densimetrico per la determin-

azione dell' emoglobina, dell' ematocrito e delle proteine del sangue nel campo ostetrico-ginecologico.)

By N. VAGLIO and G. ANZISI. *Arch. Ostet. Ginec.*, 51, 381-396, Nov.-Dec., 1946. 27 refs.

598. Function of the liver in Pregnancy Determined by W. Gros' Test. (La funzionalita epitaca in gravidanza saggiata colla prova di Walter Gros.)

By A. BONINO. *Ginecologia, Torino*, 13, 145-156, Mar. 1947. 31 refs.

599. A New Rapid Variant of Aschheim-Zondek's Test. Reiprich's reaction Modified by Kelso and Salmon-Geist. (Une nouvelle variante rapide du test de Aschheim-Zondek. Réaction d'hyperhémie ovarienne chez la rate. Réaction de Reiprich modifiée par Kelso et Salmon-Geist.)

By H. HINGLAIS and M. HINGLAIS. *Gynéc. Obstet.*, 46, 86-93, 1947. 12 refs.

600. Results of Prophylactic Work for Mothers and Children in Oslo. (Enkelte resultater av et profylaktisk forsøksarbeid for mor og barn i Oslo.)

By K. U. TOVERUD. *Nord. Med.*, 32, 2242-2246, Oct. 4, 1946. 1 fig., 5 refs.

A clinic was established in Oslo in 1939 for the supervision of the health of expectant and nursing mothers and of their children up to the age of 7 years. The staff included a paediatrician, obstetrician, dentist, and nursing personnel.

Antenatal examinations were carried out every month until the seventh month, then twice a month , and every week in the last month. If albuminuria or other conditions necessitated rest in bed, this was made possible by the provision of domestic helpers from a staff attached to the clinic. Full vitamin supplements were given, including 10 mg. of vitamin K daily. Up to the present time 1,385 women have been examined. The incidence of albuminuria was highest in 1939 and 1940 (12 and 19 per cent) and did not rise above 7 per cent in the following years; this reduction was perhaps correlated with the disappearance of meat from the diet. Infants were examined monthly up to 6 months, and then every 6 weeks up to the age of 1 year. There were 16 stillbirths in a total of 989 births (1.6 per cent); the rate for the whole of Oslo was 2.6 per cent. The infant mortality was 1.3 per cent compared with 3 per cent for the whole of Oslo.

The incidence of rickets showed a marked fall during the period reviewed; 15.9 per cent of children between the ages of 1 and 2 years were affected in 1939, while the figures for succeeding years were : 1940, 8.5 per cent; 1941, 2 per cent; 1942 and after, less than 2 per cent. Cod-liver oil in a dose containing 700 units of vitamin was given to all infants after the first month, whether breast or bottle-fed. Blood counts were carried out every 6 months in the first year and then at yearly intervals. If there was anaemia reduced iron was given. An adequate intake of iron in the diet was assured by giving vegetable purée from the fourth month onwards.

All children between the ages of 1 and 7 years received dental examinations four times a year. Their diet contained all factors necessary for satisfactory calcification, together with the minimum quantity of fermentable carbohydrate; the mothers were also instructed in suitable measures of dental hygiene to be practised on the children. A comparison of children coming under control after the first year of life with those controlled from birth showed a 50 per cent reduction in the incidence of dental caries in the latter group.

D. J. Bauer

601. A General Survey of Maternal Care in a Navy Hospital.

By G. G. GREENE. *Amer. J. Obstet. Gynec.*, 53, 669-673, Apr. 1947. 2 refs.

602. Fundamentals of Obstetric Radiology. (Fundamentos de radiología obstétrica).

By J. M. BEDOYA. *Toko-ginec. prát.*, 5, 414-426, Dec. 1946. 4 figs.

603. The Indications and Value of X-ray Examination in Obstetrics.

By H. M. EDMISON and F. G. STUART. *Manitoba med. Rev.*, 27, 224-225, Apr. 1947.

604. Supplements of Vitamin A and of Carotene During Pregnancy. Their Effect on the Levels of Vitamin A and Carotene in the Blood of Mother and of Newborn Infant.

By J. M. LEWIS, O. BODANSKY, M. C. C. LILLIENFELD, and H. SCHNEIDER. *Amer. J. Dis. Child.*, 73, 143-150, Feb. 1947. 3 refs.

These authors have drawn attention previously to the fact that the concentration of vitamin A in the blood decreases during the last 3 months of pregnancy, and that there is no corresponding drop in the concentration of carotene. The fall in vitamin-A level in the blood could not be correlated with any change in the vitamin-A content of the diet, and there was no evidence of any nutritional disturbance. This phenomenon was attributed to the demands for vitamin A made on the mother by the foetus [but no mention is made of the possible diluting effect of the increased circulatory volume, which is maximal at the thirty-sixth week and may be as much as 45 per cent above the level in the non-pregnant woman].

During the present study supplements of vitamin A or of carotene (10,000 units daily in each case) were given to 74 women during the second half of pregnancy. Plasma levels as high as, or higher than, the average for vitamin A and carotene resulted, but there was no corresponding increase in the level of these factors in the cord blood of the infants whose mothers received the supplements. Very large amounts of vitamin A (200,000 to 500,000 units) given during labour similarly failed

to produce any effect on the vitamin-A content of the infant's cord blood. Preliminary experiments on guinea-pigs suggest that the foetal liver withdraws vitamin A so rapidly from the blood that increased transmission through the placenta is not reflected in increased concentration in the blood of the newborn.   *M. Baber*

605. Nutrition in Pregnancy. (La nutrition chez la femme enceinte).

By R. SIMARD. *Union méd. Can*, **76**, 386-393, Apr. 1947. 19 refs.

606. A Study of Diets of Patients in a Prenatal Clinic with an Attempt to Correlate Dietary Adequacy with Physical Findings.

By M. W. NORTHROP and G. M. PIPER. *Northw. Med.*, **46**, 294-298, Apr. 1947.

607. Effects of Maternal Undernutrition upon the Newborn Infant in Holland (1944-1945).

By C. A. SMITH. *J. Pediat.*, **30**, 229-243, Mar. 1947. 4 figs., 20 refs.

608. The Effect of Wartime Starvation in Holland upon Pregnancy and its Product.

By C. A. SMITH. *Amer. J. Obstet. Gynec.*, **53**, 599-608, Apr. 1947. 2 figs., 23 refs.

609. Some Pathological States in Pregnancy as an Indication for Hospitalization. [In Russian.]

By S. D. ASTRINSKY. *Akush. Ginek.*, **1**, 32-35, 1947.

610. Serology and Obstetrics.

By R. T. LA VAKE. *Amer. J. Obstet. Gynec.*, **53**, 459-466, Mar. 1947.

The theory is put forward that toxaemia of pregnancy may be due to toxins resulting from incompatibility between maternal and foetal blood. The author holds the view that incompatible transfused blood is poisonous to the cells of the recipient, and that if the obscuring effects of agglutination and haemolysis could be obviated changes would be found in the recipient similar to those seen in toxaemia of pregnancy. Inherited agglutinins, he argues, represent inherited antitoxic substances which afford a modicum of protection to the female who may bear a foetus containing blood substances toxic to the type of cells she possesses. If the antitoxic substance involved is not sufficient to protect the mother and if her cells are vigorous, they will secrete more of the same antitoxic substance and the titre of the iso-agglutinin may rise. The true strength of the antitoxin may, however, be masked by the antitoxin-absorptive power of the foetal cells and antigens in solution. He discusses the reason why the human being possesses hereditary antitoxins against some substances only, and suggests that substances against which no inherited antitoxins are found may have entered the species too recently to be inheritable yet. The

Rh group is quoted as an example, and it is stated that about 30·per cent of cases of clinical erythroblastosis are associated with pregnancy toxaemia. The author found that A and B substances could bring about the same phenomena. He is now seeking specific antitoxic sera in order to treat the mother after intrapartum death of the child or postpartum eclampsia.

Three cases are · described. Mothers were of group O, Rh-positive, while fathers and children were of group A, Rh-positive. In the first case anti-A titre was 1 in 1,000 at the thirty-fourth week, when there was mild toxaemia and an accidental haemorrhage. Delivery of a living child at term was uneventful and the anti-A titre rose to 1 in 2,000 five days later. The second patient developed toxaemia and an anti-A titre of 1 in 1,000. A dead foetus was delivered at 28 weeks and the titre rose to 1 in 100,000 in 5 days. The third patient had had 2 erythroblastotic infants and had an anti-A titre of 1 in 8,000 but no toxaemia. After delivery of an erythroblastotic child, which survived after transfusion, the titre increased to 1 in 8,000,000.

[There is much theorizing on rather insecure foundation in this paper. Several other authors reporting large series of cases have been uable to correlate iso-immunization with toxaemia of pregnancy.]   *Doreen Daly*

611. Toxemia of Pregnancy and Experimental Hypertension. I. The Production and the Measurement of Experimental Renal Hypertension. II. The Etiology of Experimental Hypertension.

By S. GOLD. *Rev. canad. Biol.*, **3**, 319-355, 1946. 4 figs., 106 refs.

The title of these two papers is misleading because they are concerned with toxaemia of pregnancy only by implication. In the first paper a concise statement is given of the methods of producing experimental hypertension, together with a full bibliography. The effect of renal ischaemia in causing hypertension and its relation to nephrosclerosis is fully dealt with. The last half of the paper reviews the methods of measuring blood pressure in small animals, and an improved apparatus for the indirect determination of systolic blood pressure in the unanaesthetized rat is described.

In the second paper the mechanisms involved in the production and maintenance of experimental hypertension are reviewed. A most complete bibliography makes this article an invaluable reference for anyone concerned in the scientific study of hypertension. The mechanisms involved are discussed in terms of humoral, nervous, and endocrine agencies.   *Geoffrey Evans*

612. An Evaluation of the Karyokinetic Rhythm of Myeloid Elements in Toxaemias of Pregnancy. (La valutazione del ritmo cariocinetico degli elementi mieloidi in base allo studio delle curve cariologiche in casi di tossicosi gravidiche.)

By U. BRACALE. *Arch. Ostet. Ginec.*, **51**, 366–380, Nov.–Dec. 1946. 1 fig., 2 refs.

The second part of an investigation on the mitotic activity of the bone marrow in 21 cases of eclampsia is described. The authors have studied the percentages of the various myeloid components, the leuco-erythrogenic_activity, and the maturation of the white and red cells. Attention has been paid to the karyokinetic rhythm. Haemopoietic activity of the medulla occurs in three phases—reproduction, evolution, and migration. A table is given showing the curve of maturation ascertained by the percentages of the primitive red and white cells in the bone marrow. These are compared with the values in normal cases. A karyological curve is constructed by the study of the degrees of mitosis in the granuloblasts and erythroblasts. It is concluded that observations on karyokinesis in the myeloid elements in cases of eclampsia show that the mitotic coefficient, the quantitative expression of mitotic activity, is increased. Study of the various phases in the mitotic rhythm in the series allows the construction of a karyological curve. This curve shows general stimulation of proliferation in the white-cell-producing system. In the red-cell-producing system in cases of eclampsia the karyological curve is asymmetrical but points to an inhibition of red-cell production.

Josephine Barnes

613. A Contribution to the Study of Eclampsia.

By F. E. WHITACRE, W. M. LOEB, and H. CHIN. *J. Amer. med. Ass.*, **133**, 445-449, Feb. 15, 1947. 1 fig., 6 refs.

One hundred consecutive cases of eclampsia observed during the years 1935-1941 in Peiping Union Medical College Hospital (Group I) are compared with 100 cases observed during the years 1941-1945 in the University of Tennessee, Memphis (Group II). All the patients in Group I were Chinese; in Group II 96 were negresses and 4 white women. In spite of the difference in climate and race a remarkable similarity in detail was observed between the two groups.

Group I represented a hospital incidence of 2.2 per cent and Group II 1.2 per cent. The majority of cases in both groups occurred in the summer and autumn. The age incidence, parity, and stage of gestation were practically the same, 75 in Group I and 72 in Group II being primigravidae. In Group I 73 had not been seen before the onset of eclampsia, and in Group II 55; this emphasizes the value of antenatal care. In Group I the convulsions were in 75 cases antepartum, in 10 intrapartum, and in 15 postpartum; in Group II the corresponding figures were 77, 6, and 17. The average non-protein nitrogen in Group I was 34 mg., with uric acid 6.4 mg. per 100 ml. of blood; in Group II the respective values were 32 mg. and 6.4 mg. Twenty-two mothers died out of Group I and 14 of Group II,

while the foetal mortality was 36 in Group I and 20 in Group II. In Group I 47 patients were treated by the " combined method " of Dieckmann (*The Toxemias of Pregnancy*, St. Louis, 1941; intramuscular magnesium sulphate, barbiturates, and intravenous hypertonic dextrose are used) with 8 deaths; in Group II 58 were similarly treated, with 10 deaths. The remaining 53 patients in Group I were treated with morphine and chloral hydrate, with 2 deaths. The remaining 42 patients in Group II were treated by the " combined method " with the addition of veratrum viride, and only 1 died. Five Caesarean sections were performed in Group I, with 3 deaths, and 12 in Group II, with 1 death.

The pathology and aetiology of eclampsia are briefly discussed, with emphasis on angiospasm as the mediating cause of the changes observed. The authors think it probable that the placenta stimulates the production of pressor substances which are not sufficiently destroyed by the liver, and attempt to correlate this failure of liver function with the observation that the majority of their patients were undernourished. [This part of their paper is not supported by any new data.]

Rosenbaum and Maltby (*Arch. Neurol. Psychiat., Chicago*, 1943, **49**, 204) suggested that the electroencephalogram might be used to predict the development of eclampsia, and electroencephalographic tracings were accordingly made on 6 patients during and after convulsions. The tracings were essentially similar; those from 1 patient are reproduced, showing a gradual return to normal as the blood pressure fell after continuous caudal analgesia. The tracings between fits resembled those found in minor epilepsy, and a normal tracing was obtained on the twelfth day after delivery. The abnormal tracings were thought to demonstrate cerebral anoxaemia, which the authors consider to be due to angiospasm, although they admit that the presence of cerebral oedema may play a part.

Prophylaxis is stressed, with emphasis on a well-balanced diet and fluid and salt restriction. Relaxation of vascular spasm is considered to be the basis of any successful therapy, and in addition to the recognized treatments already described the authors have used continuous caudal analgesia (up to kidney level) in 6 patients, in all of whom diuresis was established and recovery took place.

Aileen M. Dickins

614. Eclampsia During the War. (Eklampsismus za války.)

By A. KOTASEK. *Ceskoslov. Gynaek.*, **12/26.** 144–154, 1947. 15 refs.

615. Eclampsia in Molar Pregnancy. (Eclampsia en gestación molar.)

By A. CLAVERO NUÑEZ. *Rev. esp. Obstet. Ginec.*, **5**, 222-224, Oct. 1946. 41 refs.

616. Menkin's "Menstrual Toxin" and "Necrosin", Modern Pathogenetic Conceptions of Intoxication in Pregnancy. ("Tossina menstruale" e "necrosina" di Menkin. Moderne concezioni patogenetiche della intossicazione gravidica.)

By M. TORTORA. *Arch. Ostet. Ginec.*, **51**, 397–406, Nov.–Dec. 1946. 1 fig., 24 refs.

617. The Etiology and Treatment of Hyperemesis Gravidarum.

By W. N. KEMP. *Canad. med. Ass. J.*, **56**, 409–410, Apr. 1947, 11 refs.

618. On the Treatment of Placenta Praevia.

By J. CHESTERMAN. *Med. J. Austral.*, **1**, 293–297, Mar. 8, 1947. 8 refs.

An analysis is made of the methods and results of treatment in all cases of placenta praevia admitted to the Women's Hospital, Sydney, from 1936 to 1946 inclusive (225 cases). The usual conservative methods were used for the most part with excellent results to the mothers (mortality 0.9 per cent), but indifferent results to the babies (mortality 53 per cent). Comparison is made with similar series of cases in Australia and Britain. In the decade under investigation there was a slight increase in the use of expectant treatment, with some decrease in the use of Willett's forceps and vaginal packing, but no change in the proportion treated by Caesarean section or by plugging with the half breech. The suggested management of placenta praevia in the future is outlined, though there appears to be some lag behind the treatment advocated in Britain to-day.

[The application of Willett's forceps and plugging with the half breech are still advocated for marginal placenta praevia. No mention is made of the value of inspection of the cervix when the patient is first admitted to hospital.]

D. M. Stern

619. Premature Detachment of the Placenta in Practice. (O descolamento prematuro da placenta na prática.)

By A. LEITE CONDE. *Rev. Ginec. Obstet.*, **1**, 268–271, Mar. 1947. 5 refs.

620. The Rh Factor in Abortion.

By A. B. HUNT. *Amer. J. Obstet. Gynec.*, **53**, 467–473, Mar. 1947. 9 refs.

The incidence of single spontaneous abortions does not seem to be influenced by the presence or absence of the Rh factor. The incidence of stillbirth and neonatal deaths, however, is higher among Rh-negative women than among Rh-positive. The number of women in a group of 93, with a history of recurrent abortion, whose blood did not contain the Rh factor, was somewhat higher than would be the case in the general population [18.3 per cent in this series]. There seems to be no striking increase in the frequency of abortion or miscarriage after the occurrence of

erythroblastosis foetalis [11.5 per cent miscarriage rate after erythroblastosis quoted from a series by Race *et al.* Numbers are insufficient to be conclusive in the author's series]. On the other hand, there is a striking increase in the casualties of late pregnancy among Rh-negative women. [4.5 stillbirths compared with 0.9 per cent.] Data concerning a small series of 25 women who gave birth to a normal child and then began to have abortions and miscarriages are analyzed; 23 Rh-negative women had more than one unproductive pregnancy compared with only 2 who were Rh-positive. In this series there were fewer Rh-negative women than are found, comparatively speaking, in the general population.

The Rh factor has possibly been over-emphasized as a cause of abortion and miscarriage at the expense of more common causes—such as dysfunction of the ovaries, pituitary, thyroid, and, possibly, the testes of the husband. An Rh-negative woman subject to habitual abortion may be permitted to attempt another pregnancy in the more nearly ideal physiological environment that proper therapy may provide. *Doreen Daley*

621. Sulphonamide Treatment of Febrile Abortion. (Die Sulfonamidbehandlung der fieberhaften Fehlgeburt.)

By K. J. ANSELMINO. *Dtsch. med. Wschr.*, **72**, 63–66, Feb. 14, 1947.

The introduction of the new and powerful sulphonamide combination, "De-Ma" [debenal-marbadal, apparently a combination of sulphadiazine with a marfanil (sulphamylon) derivative] came at a critical time for German gynaecology, since it coincided with a large increase in the number of cases of abortion admitted to the author's clinic in Wuppertal. The incidence of puerperal infection again proved a menace. The death rate from febrile abortion had steadily fallen in this clinic between the years 1931 and 1939, evidence of the value of sulphonamide treatment, introduced during these years, in such cases. The author reports his latest results (1945-1946) with De-Ma.

The management of cases is described. Digital evacuation of the uterus is performed and sulphonamides are given both by mouth and locally, various preparations and derivatives of this group of drugs being employed. De-Ma has been the most recently employed and has given satisfactory results. The aims of treatment are to reach a high concentration in the blood (20 to 30 mg. per 100 ml.) and to maintain this level to obtain the maximal bacteriostatic effect. In addition, 3 to 5 g. are introduced into the uterine muscle and the neighbouring tissues. It has been shown that sulphonamide so introduced appears in the urine within 1 hour. De-Ma and another sulphonamide combination, MPE (marfanil, sulphanilamide, sulphathiazole), are effective against both aerobic

and anaerobic infections. 'It is emphasized that for the best effect an adequate dose must be given and high doses in severe cases. For a woman weighing 60 to 70 kg., a dose of 10 to 14 g. daily is required; this is maintained for 3 days, and then reduced in accordance with the clinical picture. Recommendations for the use of sulphonamides in domiciliary treatment of these cases are made. Dramatic results are often seen and the author claims that his results are proof of the powerful activity of De-Ma.

[The value of sulphonamide treatment for septic abortions, provided the infecting organism is sulphonamide-sensitive and an adequate dose is given, is well known. De-Ma does not appear to have been used in Britain and there is, therefore, no standard of comparison with our potent new sulphonamides such as sulphadiazine and sulphamezathine.]

Josephine Barnes

622. **Treatment of Febrile Abortion.** (Le traitement de l'avortement fébrile.)

By A. TURRETTINI. *Gynaecologia, Basel,* 123, 201–210, Apr. 1947. 13 figs.

623. **Specific Treatment (Antiluetic) in Cases of Habitual Abortion, Missed Abortion, Partus Prematurus, and Stillbirth.** [In English.]

By A. SADOVSKY and S. KAPLAN. *Acta. med. orient.,* 6, 95–98, Mar. 1947. 10 refs.

624. **Torsion of the Pedicle of an Ovarian Cyst after Abortion.** (Torção pedicular de quisto ovariano no post-aborto.)

By L. R. L. DE GOUVEA. *Arch. brasil. Med.,* 36, 399–402, Sept. and Oct., 1946.

625. **Normal and Ectopic Pregnancy and Incomplete Abortion. Critical Study of the use of Hysterosalpingography for Diagnostic Purposes.** (Gravidez eutópica, ectópica e abortamento incompleto - estudo crítico sôbre o emprêgo da histerossalpingografia como recurso diagnóstico.)

By A. CAMPOS DA PAZ FILHO. *Med. Cirurg. Farm.,* No. 130/131, 121–133, Feb.–Mar., 1947. 17 figs., 25 refs.

626. **Abdominal Amniotic Puncture as a Valuable Aid to Differential Diagnosis.** (Die abdominale Amnionpunktion als wertvolles differentialdiagnostisches Hilfsmittel.)

By F. HOFF. *Wien. med. Wschr,* 97, 96–99, Feb. 22, 1947. 2 figs., 17 refs.

The diagnosis of hydatidiform mole is often difficult, especially in the first half of pregnancy. The differential diagnosis may be from acute hydramnios or multiple pregnancy. In most cases of hydatidiform mole the uterus is larger than would be normal for the period of amenorrhoea and slight haemorrhage often occurs. In some cases, however, the uterus is smaller than expected. The diagnosis must be made from threatened abortion. There are cases where the Aschheim-Zondek reaction, usually positive in dilutions of 1 in 200 or more in cases of hydatidiform mole, is negative. X-ray examination may be helpful.

In cases where the diagnosis is in doubt puncture of the amniotic sac through the anterior abdominal wall may be helpful. This method is contraindicated where there are acute or subacute infective lesions of the pelvic organs or peritoneum, or adhesions, or a ventro-fixation operation has been performed. Local analgesia is administered. The puncture needle is about the size of a lumbar-puncture needle. The site chosen is in the midline below the umbilicus. The tissues are infiltrated with about 2 ml. of procaine. An assistant steadies the uterus by pressure on the fundus; the puncture needle is attached to a 10 ml. syringe and pushed into the uterine cavity. In cases of hydramnios or twins amniotic fluid will be aspirated, but in cases of hydatidiform mole, where aspiration is negative, the contents of the needle must be fixed and stained with haematoxylin and eosin for microscopical examination of tissue obtained. The patient should be kept at rest for at least an hour after the puncture, and, if an out-patient, she is advised to remain in bed until the next morning. In other cases the patient should be kept in bed for 24 hours to avert the risk of abortion. It is claimed that this method is safe, simple, and can be used when the diagnostic aids of a modern clinic, such as X-rays and hormone analyses, are not available.

Josephine Barnes

627. **Malaria and Abortion.** (Paludisme et avortement.)

By —. LAFFONT and —. EZES. *Gynéc. Obstét.,* 45, 818–822, 1946. 2 refs.

628. **Action of Molar Gonadotrophin on the Ovary, Persisting Two Months after the Expulsion of the Mole.** (Action permanente des gonadotrophines molaires sur l'ovaire, deux mois après expulsion d'une môle.)

By J. BOY and J. CHEYMOL. *Ann. d'Endocrinol.,* 8, 12–16, 1947. 5 figs., 1 ref.

The finding of 50,000 units of gonadotrophin per litre of serum in a patient 2 months after the expulsion of a mole led to a hysterectomy and the examination of the uterus and ovaries. The uterus, in spite of the high gonadotrophin titre, merely contained two small intramuscular nodules of placental tissue, no metastases were apparent.

The ovaries, which were somewhat enlarged, did not contain the usual lutein cysts but presented an appearance similar to those of the rabbit with an intensely positive Friedman reaction. The surface was nodular with numerous haemorrhagic cysts. Sections showed follicles in different stages from the haemorrhagic, full of blood-clot, to the fully developed normal corpus luteum. This reaction in response to the persistent action of chorionic

gonadotrophin resembles that seen by the authors in rabbit ovaries examined several months after the animals had been used to demonstrate a positive Friedman reaction.

S. S. B. Gilder

629. **Clinical Features of Hydatidiform Mole.** (Clínica de la mola hidatídica.)

By J. M. BEDOYA. *Rev. esp. Obstet. Ginec.*, **6**, 1–19, Jan.–Feb., 1947. 6 figs., 43 refs.

630. **Hydatidiform Mole.** (Mola hidatiforme.)

By R. SALINAS RIVERO. *Arch. méd. méx.*, **5**, 46–53, Feb., 1947. 4 refs.

631. **Embryonal Teratoma.** (Teratoma embrionario.)

By P. BARATA RIBEIRO and J. BICA. *Obstet. Ginec. lat.-amer.*, **5**, 103–110, Mar.–Apr., 1947. 8 figs.

632. *Schedule of Material of the Gynaecological and Obstetrical Institute of the Armenian S.S.R. on Premature Delivery During 25 years.*

Akush. Ginek., **1**, 25–32, 1947.

633. **Dysgerminoma and Pregnancy.**

By H. SCHNEIDER and M. VESELL. *Amer. J. Obstet. Gynec.*, **53**, 688–691, Apr. 1947. 2 figs., 11 refs.

634. **Bilateral Dermoid Cysts, Uterine Fibroids, and Pregnancy.**

By M. BERLIND. *Amer. J. Obstet. Gynec.*, **53**, 692–693, Apr. 1947. 1 fig., 1 ref.

635. **Irradiation of the Ovary and its Effect on the Offspring.** (L'irradiazione dell' ovaio e la sua azione sulla discendenza.)

By F. CRAINZ. *Ginecologia, Torino*, **12**, 383–461, Dec. 1946. Bibliography.

636. **A Case of Spontaneous Rupture of the Rectus Abdominis during Pregnancy.** (Sur un cas de rupture spontanée du grand droit de l'abdomen au cours de la grossesse.)

By J. POITEAU and P. HOULNE. *Gynéc. Obstét.*, **45**, 822–824, 1946.

637. **Carcinoma of the Lung in Pregnancy.** (Il cancro del polmone in gravidanza.)

By L. de GIORGI. *Arch. Ostet. Ginec.*, **51**, 329–348, Nov.–Dec., 1946, 5 figs., 41 refs.

638. **Heartburn of Pregnancy.**

By M. SEIFE. *J. Bowman Gray Sch. Med.*, **5**, 49–55, Mar. 1947. 32 refs.

639. **Heart Disease and Pregnancy.** [In English.]

By G. NYLIN. *Cardiologia, Basel*, **11**, 151–174, 1946–1947. 7 figs.

The author uses his special method of measuring the heart volume and finds that with a volume of less than 500 ml per square metre of body surface a successful pregnancy is possible whatever the valvular lesion. In those with volumes above that figure he estimates the oxygen debt accumulated after exercise by measuring the metabolic rate after the patient has walked or run up a staircase. He finds that the normal upper limit after light, moderate, and heavy work is +40 per cent, +70 per cent, and +100 per cent respectively. Seven illustrative cases are given. The first patient with mitral stenosis had a normal heart volume and oxygen debt and accomplished pregnancy without difficulty. Three patients had congenital heart disease. The first, with a patent interventricular septum and complete heart-block, had a heart volume of 520 ml. per sq. m. and oxygen debt of 160. She required digitalis and rest in bed but had a natural delivery 4 weeks prematurely. The second, with a patent ductus arteriosus, had a normal heart volume and oxygen debt, and pregnancy was uneventful. In the third patient, with Fallot's tetralogy, the pregnancy was terminated artificially. Of the last 3 patients, 2 had mitral stenosis and the 3rd a bundle-branch block. The heart volumes varied from 540 to 850 ml. per sq. m. In all 3 pregnancy was allowed to continue under careful supervision. Two of the lesions became decompensated during pregnancy, but all patients managed labour without undue difficulty.

This article confirms the long-established rule that the size of the heart in pregnancy matters more than the valvular lesion.

C. W. Bain

640. **Cardiopathy and Pregnancy.** (Cardiopatia e gravidez.)

By R. SEGADAS. *Hospital, Rio de Janeiro*, **31**, 525–545, Apr. 1947.

641. **Heart Disease, Pregnancy and Birth.** (Herzkrankheiten, Schwangerschaft und Geburt.)

By J. FROEWIS. *Wien. klin. Wschr.*, **59**, 200–203, Apr. 4, 1947. 14 refs.

642. **Indication for Artificial Termination of Pregnancy from the Cardiologist's Point of View.** (Indikace preruseni tehotenstvi se stanoviska kardiologa.)

By P. LUKL. *Ceskoslov. Gynaek.*, **12**(26), 67–80, 1947. 35 refs.

643. **The Influence of Pregnancy on the Heart from the Clinical, Radiological, and Electrocardiographic Point of View.**

By J. I. ARKUSSKY. *Akush. Ginek.*, **1**, 11–15, 1947.

644. **Pregnancy and Stenosis of the Aortic Isthmus.** (Schwangerschaft und Stenose des Isthmus Aortae.)

By G. A. LINDEBOOM. *Gynaecologia, Basel*, **123**, 238–242, Apr. 1947. 1 fig., 2 refs.

645. **Pernicious Anemia of Pregnancy.** [In English.]

By G. A. LINDEBOOM. *Gynaecologia, Basel,* 123, 175–185, Mar. 1947. 2 figs., 10 refs.

646. **Two Cases of Neurological Disease Complicating Pregnancy; Disseminated Sclerosis, Pseudoparalytic Myasthenia Gravis.** (Su due casi di affezioni neurologiche complicanti la gravidanza, sclerosi a placche-miastenia grave pseudoparalitica.)

By L. GIANAROLI. *Riv. ital. Ginec.,* 29, 267–280, 1946. 43 refs.

647. **Pathogenesis of Herpes Gestationis.** (A propos de la pathogènie de l'herpès gestationis.)

By R. RAYNAUD and J. R. D'ESHOGUES. (*Ann. d'Endocrinol.,* 7, 238–242, 1946. 4 refs.

A case of herpes gestationis which occurred in the fifth month of the seventh pregnancy is described. The herpes appeared as a symmetrical generalized bullous erythema with an eosinophil count of 27 per cent. Immediately after childbirth the erythema almost disappeared, but reappeared 6 months later at the same time as the menstruation. Testosterone, 10 mg. daily, was given, and the rash improved on the second and disappeared completely on the fourth day. The authors believe that the times of the appearance of the herpes (towards the end of the pregnancy and later with the resumption of the menstrual cycle) prove its connexion with a comparative excess of oestrogens and a lack of progesterone.

H. Herxheimer

648. **A Case of Dermatosis, Twin Pregnancy, Foetal Death and Superfoetation.** (Dermatosis. Embarazo gemelar. Muerte fetal. Superfetación.)

By —. MARINO-PENSADO. *Toko-ginec. práct.,* 5, 393–404, Dec. 1946. 5 figs., 17 refs.

649. **Acute Anterior Poliomyelitis during Pregnancy.** (Poliomyelitis anterior acuta in gaviditate.)

By R. GRELLAND. *Nord. Med.,* 33, 620–625, Mar. 7, 1947. 1 fig., 31 refs.

A report is given on 10 cases of acute anterior poliomyelitis complicating pregnancy with short clinical notes on each. Reference to the literature shows that comparatively few cases of this combination have been reported. In the series under analysis the ages of the patients ranged from 20 to 41, all but one being under 31 years of age. Four deaths occurred, all in cases developing the illness in the last 3 months of pregnancy. There was a high incidence of respiratory paralysis—6 cases out of the 10. The Scandinavian literature contains 9 previous reports of this condition, totalling 48 cases. The average age was 25, and the disease occurred more commonly in the last 3 months of pregnancy. Fifteen out of the total 58 patients (26 per cent) had respiratory paralysis. Of 35 patients who went into labour, delivery was normal in 32 (91 per

cent); in 3 cases (9 per cent) Caesarean section was performed. In 30 cases (52 per cent) the patient gave birth to a normal infant. The occurrence of intrauterine infection of the foetus was not definitely established. Caesarean section was indicated only in very severe cases, particularly if respiratory paralysis was present.

The total mortality was 26 per cent. Of 29 cases in the first 6 months of pregnancy the mortality was only 3.4 per cent, whereas of 29 cases in the last 3 months of pregnancy it was 48 per cent. The prognosis is therefore poor when the disease occurs in the last 3 months of gestation.

J. W. S. Lindahl

650. **Massive Intra-abdominal Hemorrhage of Renal Origin, Complicating Pregnancy, with Recovery.**

By W. C. SCRIVNER. *Urol. cutan. Rev.,* 51, 81–82, Feb. 1947.

651. **Effect of Diabetes Mellitus on Foetus.**

By H. BAHRY. *J. Obstet. Gynaec., Lahore,* 8, 41–46, Apr. 1947.

652. **The Existence of a State of Latent Tetany in Pregnancy.** (Sull' esistenza di uno stato di tetania latente in gravidanza.)

By W. BENOLIEL. *Riv. ital. Ginec.,* 29, 314–328, 1946. 23 refs.

653. **On the Wasserman and Kahn Reactions During Pregnancy.** [In English.]

By K. PENTTINEN. *Acta. obstet. gynec. scand.,* 27, Suppl. 3, 1–114, 1947. Bibliography.

654. **The Management of Pregnancy and Tuberculosis.**

By G. SCHAEFER. *Surg. Clin. N. Amer.,* 27, 461–465, Apr. 1947. 5 refs.

655 **Pregnancy and Malaria.** (Grossesse et Malaria.)

By —. LEVY DU PAN. *Gynéc. Obstét.,* 45, 816–818, 1946.

656. **Clinico-statistical Data in 436 Cases of Ectopic Pregnancy.** (Considerazioni clinico-statistiche sopra 436 casi di gravidanza ectopica.)

By A. FUMAROLA. *Ginecologia,* 13, 49–83, Feb. 1947. 39 refs.

The author presents a detailed clinical and statistical survey of 436 cases of ectopic gestation collected from the Obstetrical and Gynaecological Clinic of the University of Rome between the years 1936 and 1943. Extremely detailed tables are given and the material is classified under the following main headings: past and recent history, pathological anatomy, operation performed, postoperative course, and remote prognosis. A special section is devoted to errors of diagnosis.

Points of special interest from the tables are as follows: Of the patients, 95 per cent were married. Menstruation had been regular in 65 per cent, irregular in 34 per cent. Of the parous patients,

31 per cent were uniparae and 69 per cent multiparae. In 30 per cent there was a history of pelvic inflammatory disease or of a previous abdominal operation. The gestations were right-sided in 52 per cent, left-sided in 47 per cent. The corpus luteum was on the same side in 72 per cent, on the opposite side in 24 per cent, bilateral in 0.45 per cent, and not located in 2.76 per cent. Three cases treated by colpotomy are excluded.

There were 421 cases of tubal gestation. Of these, 303 (72 per cent) were ampullary and 243 (79 per cent) terminated in tubal abortion, while 20 per cent terminated in rupture of the tube. In 97 cases (23 per cent of the total) the pregnancy was in the isthmus; 36 (37 per cent) of these cases terminated in abortion and 60 (61 per cent) in rupture. Thirteen cases of interstitial pregnancy all ended in rupture of the tube. There were 5 cases of long-standing ectopic pregnancy, with 1 case of a macerated foetus after 5 months' amenorrhoea, intraligamentary pregnancy, and suppuration. There was 1 case of maceration of the foetus with putrefaction of the ovular sac, diagnosed after 9 months' amenorrhoea, and 1 case of secondary abdominal pregnancy. Angular pregnancy occurred in 4 cases, 2 ending in abortion and 2 in rupture of the uterus. In 3 cases, pregnancy occurred in an atretic uterine cornu and ended in uterine rupture with haemoperitoneum. There were 4 cases of fimbrial pregnancy and 1 of ovarian pregnancy.

The two main symptoms—pain and haemorrhage—occurred simultaneously in 47 per cent of cases. Bleeding preceded pain in 21 per cent, while pain preceded bleeding in 31 per cent. Unilateral salpingo-oöphorectomy, often combined with other procedures, was performed in 81 per cent of cases, while unilateral salpingectomy was done in 15 per cent. The post-operative period was complicated in 7 cases, and there were 4 deaths. Details of the remote course are given. The chief complaints were of irregular or painful periods. In 42 cases an error of diagnosis was made; these are given in detail. The author concludes that the commonest aetiological factor in ectopic gestation is previous pelvic inflammatory disease.

[This long and detailed article is a valuable contribution to the literature of ectopic gestation. It is not possible to do justice to the wide scope of the work in an abstract.]

Josephine Barnes

657. Ectopic Pregnancy (A Contribution to the Problem of the Decidual Transformation of the Endometrium in the Presence of Ectopic Pregnancy.)
By W. OPPENHEIMER. *Harefuah*, **32**, 35–38, Feb. 2, 1947. 55 refs.

658. Ectopic Pregnancy and Genital Hypoplasia. (Prenhez ectópica e hipoplasia genital.)
By S. RUAS MARTINS. *Rev. méd. munic.*, **9**, 133–149, Oct.–Dec. 1946. 14 figs.

659. Combined Intrauterine and Extrauterine Pregnancy.
By G. SCHAFFER. *Surg. Clin. N. Amer.*, **27**, 467–470, Apr. 1947. 8 refs.

660. Uterine Pregnancy with Intramembraneous Foetal Development in the Free Peritoneal Cavity after Rupture of the Uterus in a Caesarean Section Scar. (Graviditas uterina s intramembranosním vyvojem plodu ve volné dutine -brisní po rupture jizvy po císarském rezu.)
By J. VLTAVSKY. *Ceskoslov. Gynaek.*, **12** (26), 86–94, 1947. 12 refs.

661. A Case of Intraligamentary Pregnancy at Term. (Embarazo intraligmantario a termino. Reporte de un caso.)
By J. A. RODON BADELL. *Rev. Méd. quirúrg. Oriente.*, **8**, 28–33, Mar. 1947. 3 figs., 9 refs.

662. A Case of Ovarian Pregnancy. (D'un cas de *grossesse ovarienne.*)
, By R. GUENIN. *Gynaecologia, Basel*, **123**, 167–174, Mar. 1947. 4 figs., 11 refs.

663. Genesis of Primary Abdominal Pregnancy. (Per la genesi della gravidanza abdominale primitiva.)
By L. DE GIORGI. *Arch. Ostet. Ginec.*, **92**, 1–16, Jan.–Feb. 1947. 4 figs., 16 refs.

664. Features Resembling Early Pregnancy after Administration of Follicular and Corpus Luteum Hormones in Large Amounts. (Frühschwangerschaftähnliches Bild nach Verabreichung grosser Follikel-und Gelbkörperhormonmengen.)
By A. SZARKA. *Gynaecologia*, **122**, 338–346, Dec. 1946. 1 fig.

Rare cases have been described in which the usual features of pregnancy occur, such as cessation of menstruation, uterine enlargement, and softening of the genital tract, but in which pregnancy is not found. In some cases the pregnancy tests have been positive and the endometrium shows the changes of early pregnancy. Earlier observers thought that in these cases the ovum had been fertilized but not embedded. Later, Meyer thought that the condition could arise without fertilization of the ovum and be due to the continued growth of the corpus luteum usually with cyst formation. Several cases have been described with the features of early pregnancy, with no uterine or extrauterine pregnancy, but with a persistent corpus luteum or luteal cyst. A corresponding condition is known to occur in animals and can be produced experimentally, for example, in the rat by irritation of the cervix or injection of gonadotrophin.

The author believes that the abnormal persistence of the corpus luteum is the cause of this condition. Clinical evidence supports this view but there is as yet no proof. He endeavoured to produce these features in an ovariectomized woman with

hormone therapy. The patient, aged 43, had had a bilateral ovariectomy eight years before for a tubo-ovarian abscess. Endometrial biopsies and vaginal smears confirmed the absence of ovarian tissue, and 14.5 mg. of oestradiol benzoate was required to produce endometrial proliferation up to 15 to 16 days of the cycle (previously reported). In this case, in the course of about 3 months, 4 million I.U. of follicular hormone followed by 440 mg. of progesterone in the last 40 days were given. Symptoms of pregnancy resulted, namely, morning sickness, faintness, swelling of the breasts, softening of the vagina. After the follicular hormone had been reduced bleeding and painful colic occurred with the passage of an endometrial cast.

Microscopical examination showed a marked decidual reaction corresponding to the second month of pregnancy but with hypofunction of the glands; the stroma was fully developed but the glandular elements less so, and development was irregular. Why the above changes were not uniform in the stage of development is not clear but it appears that the dose of progesterone was not adequate for full development. To produce the changes of pregnancy both oestrin and progesterone must be given in certain quantities and with certain time relations. It is essential to continue giving oestrin with progesterone or bleeding will occur. The amount of oestrin required to prevent bleeding is not known, but in this case it appeared that 5 mg. (50,000 I.U.) daily were necessary.

L. W. Lauste

665. **Incomplete Clinical Form of Total Rupture of the Uterus.** (La forma clínica incompleta de la rotura total del útero. Consideraciones sobre un caso.)

By D. R. GARCIA PASTOR. *Rev. esp. Obstet. Ginec.*, 5, 348–359, Dec. 1946. 5 figs., 43 refs.

LABOUR

666. **Prognosis of Parturition.** (Pronóstico del parto.)

By J. MILLAN SANTOS. *Toko-ginec. práct.*, 6, 65–94, Mar. 1947.

667. **The Conduct of Normal Labour.** (Quelle doit être la conduite de l'accoucheur pendant l'accouchement " dit normal ".)

By J. SMOECK, M. ROCMANS, and O. GOSSELIN. *Gynéc. Obstét.*, 45, 680–708, 1946. 42 refs.

668. **The Second Stage of Labor; Internal Rotation.**

By L. A. CALKINS. *Amer. J. Obstet. Gynec.*, 53, 488–493, Mar. 1947. 1 ref.

An attempt was made to determine the time of internal rotation of the head of the baby in relation to the stage and duration of labour in 2,900 primiparae and 2,500 multiparae, the time of rotation apparently being estimated clinically by various observers. It is stated that early rotation is more frequent in multiparae than in primiparae, but it is unrelated to the size of the head. It is alleged to be influenced also by parity and the character of uterine contractions.

D. M. Stern

669. **Constriction Ring Dystocia.**

By M. P. RUCKER. *Amer. J. Obstet. Gynec.*, 52, 984–992, Dec. 1946. 27 refs.

The author discusses 202 cases of constriction ring dystocia encountered in 13,575 deliveries. He defines constriction ring dystocia as that form of soft part dystocia characterized by the formation within the uterus of one or more bands of uterine muscle. These bands form opposite depressions in the foetal ovoid and may occur at any level. A Bandl's retraction ring on the other hand is located at the junction of the actively contracting portion of the uterus with the lower uterine segment. According to the author's figures the incidence of constriction ring dystocia is 1.67 per cent. The impression that the condition is rare may be due to the fact that many cases are overlooked.

The diagnosis can only be made with accuracy by feeling the ring with the hand in the uterus; this was done in 199 of the cases. A ring may be suspected, however, when there is no obvious cause for failure of labour to progress in spite of good " pains." The pains are said to be characteristic in that the painful sensation continues after palpable hardening of the uterus has passed off. While such pains are suggestive they are not, in the author's opinion, pathognomonic. If, upon vaginal examination, the cervix hangs loosely about the presenting part the presence of a ring should be suspected. The condition is in the nature of a fatigue phenomenon analogous to the spasms which sometimes occur in the striated muscles of swimmers and runners. Contrary to expressed beliefs, the author found no significant increase in the frequency of the condition in induced labours, nor was the incidence greater in those patients who received pituitrin during the first stage of labour. On the other hand, the presence of unfavourable factors —such as primigravidity, increased age, abnormal presentation, and borderline contraction of pelvis —appeared to influence the onset. A favourable presentation occurred in only 30 per cent of the cases. Of the patients 134 were primigravidae, and the average age was 28.4 years, a figure about 2 years higher than the average for the whole series. The type of pelvis was recorded in 139 cases: 87 were normal, 28 were funnel, 18 were justo-minor, 4 were flat, and 2 were flat rachitic pelves.

The condition is liable to occur at any time during the three stages of labour. When it is suspected during the first stage either sedatives or magnesium sulphate intravenously should be given, and sleep encouraged. After the patient has rested labour tends to progress satisfactorily. When the ring appears late in the second stage or when the cervix

is fully dilated two lines of treatment are recommended. After the patient has rested, the ring will relax, but it is better to cause the ring to relax so that the child can be delivered as soon as possible. Dragging a baby through an unrelaxed ring is not good obstetrics. The ring can be made to relax in various ways. Deep anaesthesia with chloroform or ether has been recommended, but in the author's experience neither is satisfactory. Spinal analgesia failed to have any effect in 10 cases in which it was tried. The author has had no experience with either amyl nitrite or magnesium sulphate as preliminaries to delivery, but excellent results have been claimed for both drugs. Adrenaline, 1 in 1,000, administered in 5 to 8 minim (0.32 to 0.52 ml.) doses has been the most reliable agent so far, and was used in 150 cases. In 7 it was necessary to give a second injection and in 8 the drug failed to relax the ring. An effect should appear in 3 to 5 minutes. In 20 cases encountered before the advent of *adrenaline treatment, inhalation anaesthesia was* given and manual dilatation performed. With this treatment 1 mother and 9 babies died. Since adrenaline has been used there have been no maternal deaths and the foetal mortality rate has been 17.5 per cent. Eleven infant deaths occurred in the first 23 cases. As experience with adrenaline has grown the results have improved.

R. L. Hartley

670. Action and Application of Carbaminoylcholine in Obstetrics. (Las acciones y las aplicaciones obstétricas de la carbaminoilcolina.)

By F. SANZ SANCHEZ and J. M. BAYO. *Farmacoter. actual,* 4, 18–25, Jan. 1947. 15 figs., 12 refs.

As the literature on the obstetrical application of carbaminoylcholine is scanty the authors have reviewed the results obtained in veterinary obstetrics, and give the results of their own investigations. Carbaminoylcholine is a parasympathetic stimulant which produces almost all the actions of acetylcholine in greater or lesser intensity. It is a stable, white substance, dissolving in water with a neutral reaction; it can be boiled without loss of activity and can therefore be given safely by subcutaneous or intramuscular injection. It causes a fall in blood pressure, stimulates the movements and secretory activity of the alimentary canal, increases the gastric acidity, produces miosis and a fall in the intraocular pressure, and stimulates the uterus, bladder, and ureters. It also has a nicotine-like action, and when given in large doses in the decerebrate cat produces a marked secretion of adrenaline with a rise in blood pressure. Toxic effects, which can be treated with atropine, consist of a haemorrhagic gastro-enteritis, nephritis, miosis, and salivation. It is also effective by the mouth, but larger doses are then needed; it differs in this respect from acetylcholine, which has little action when given by mouth.

In the cow, its use by the subcutaneous or epidural route strongly stimulates the uterus in cases of uterine atony and placental retention. It has also been given in catarrhal nephritis and pyometritis. By producing pelvic congestion it is of value in the treatment of sterility. The drug is successful in placental retention in the sow, and also when milk secretion is deficient or there is a mastitis. It has been used as a uterine stimulant in the treatment of sterility in the mare. The effects are similar in the ewe and the goat, but the oral method of administration is preferable because severe hypotension is produced by parenteral injections. In the bitch the drug has been of value in placental retention, uterine atony, different kinds of metritis, and defective lactation.

In their own experiments the authors have compared its effects with those of pituitrin and ergotamine, and have studied the effects of its administration by different routes and its action on the smooth muscle of the alimentary canal and on blood pressure. *The oxytocic effects are obtained with dilute* solutions and even in fatigued muscle, and are greater than those of ergotamine. Further contraction can be obtained in uterine muscle already contracting under the influence of ergotamine. The effects vary with the species of animal and the dose employed, but in general, are greater than those of pituitrin. When the drug is given subcutaneously the fall in blood pressure is less and recovery slower than when it is given intravenously. By the lumbar or epidural route the fall is also less marked and the return to normal slower than when the drug is given subcutaneously. The return to normal of the blood pressure after injection of prostigmin and carbaminoylcholine is also slower than after acetylcholine, owing to the rapid destruction of the latter. Finally, prostigmin has less action on the intestinal or uterine muscle than carbaminoylcholine. The disadvantages of effects on other systems can be partly avoided by epidural injection. The authors conclude that this drug is of value in both experimental and domestic animals for its action on uterine muscle.

Bryan Williams

671. Pituitary Extract in Uterine Inertia: Is it Justifiable?

By N. J. EASTMAN *Amer. J. Obstet. Gynec.,* 53, 432–441, Mar. 1947.

This article is a preliminary report from the Johns Hopkins University and Hospital on the use of pituitary extract in some cases of uterine inertia. The author states that, " Having been brought up to believe that the administration of pituitary extract before the birth of the baby constitutes the most heinous of obstetric sins, but during the past 5 years having observed its ultra-cautious use in several hundred cases of uterine inertia, I am inclined to believe that the balance lies slightly in favour of pituitary extract—provided, and provided again, that certain rigid rules be observed."

Pituitary extract (pituitrin) was used in doses of ½ to 1 minim (0.03 to 0.06 ml.) repeated in 30 minutes. The number of injections ranged from 1 to as many as 35; the average was 3 or 4. Uterine inertia is defined as follows: " In the first stage, sluggishness of uterine contractions (after true. labour has begun) of such a degree that (1) the cervix shows no change over an eight-hour period, and (2) the uterine wall is easily indentable at the acme of each pain; in the second stage, sluggishness of uterine contractions of such a degree that the head neither rotates nor descends over a two-hour period with a uterine wall which is easily indentable at the acme of each pain."

The most notable benefit claimed is a dramatic reduction in the incidence of mid-forceps deliveries, from 1 in 200 to 1 in every 1,000 where pituitrin was used. The author believes that this represents an important saving in foetal life and a reduction in the incidence of maternal trauma. A case of uterine rupture is reported in some detail. Before administration of pituitrin (the initial dose must not exceed ½ minim) the labour must be at a standstill after 3 to 4 cm. dilation; there must be no mechanical obstruction to easy delivery, as attested by every type of evidence possible; the condition of the foetus must be good; the obstetrician must observe and time the first contraction after administration of the drug; and when there is doubt that a given case meets the above criteria pituitary extract should not be given. Finally, patients who have had 4 or more pregnancies must not be given the drug because their uteri rupture more readily.

[This article gives what is probably a true assessment of the position of pituitary extract in the treatment of uterine inertia. It is of special importance in that it points out clearly the attendant dangers.]

G. Gordon Lennon

672. **Amphetamine in Labour.** (Da anfetamina no trabalho de parto.)

By G. DE CARVALHO SERRANO and E. R. TRAVASSOS. *Rev. Ginec. Obstet.*, 1, 183–187, Feb. 1947. 9 refs.

673. **Pregnancy and Delivery with Excessive Size of the Foetus.** (Prenhez e parto com feto de volume excessivo.)

By J. AMORIM, O. LACRETA, and L. ENDRIZZI. *An. brasil. Ginec.*, 22, 393–401, Nov. 1946. 13 refs.

674. **The Inverted Forceps Grip and its Use in Frontal Dystocia.** (La presa invertida de fórceps y su utilidad en la distocia de frente.)

By D. A. PLANELL. *Rev. esp. Obstet. Ginec.*, 5, 338–341, Dec. 1946.

675. **A Rare Case of Obstruction in Childbirth.** (Rzadki przypadek przeszkody porodowej.)

By A. KELHOFFER. *Przegl. Lek.*, 2, 466–470, Oct. 31–Dec. 1, 1946. 3 figs.

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676. **Dystocia due to Severe Cervicovaginal Cicatrization.** (Distocia por cicatrizacion viciosa cérvicovaginal.)

By G. VAUTRIN and E. SANCHEZ ROJAS. *Rev. méd. cubana.*, 58, 82–95, Feb. 1947. 5 figs.

677. **Brow Presentation : A Technical Trick.** (Apresentação de fronte. Artificio de técnica.)

By L. R. L. DE GOUVEA. *An. brasil. Ginec.*, 23, 36–39, Jan. 1947.

678. **Study of Multiple Pregnancy.** (Estudio sobre el embarazo múltiple.)

By E. MARTINEZ CARMONA and J. A. QUERALT BALLESTER. *Rev. esp. Obstet. Ginec.*, 6, 25–32, Jan.–Feb., 1947. 10 refs.

679. **Hydramnios with Dangerous Postpartum Intraperitoneal Haemorrhage due to Rupture of the Liver.** (Hydramnion mit lebensbedrohlicher Blutung in die Bauchhöhle post partum infolge Leberrupture.)

By F. WALLAU. *Z. Geburtsh. Gynäk.*, 128, 13–17, Mar. 1947.

680. **Acute Puerperal Inversion of the Uterus with Two Cases Seen at Cesarean Section.**

By D. F. KALTREIDER and G. B. WEST. *Bull. Sch. Med. Maryland*, 31, 144–150, Apr. 1947. 22 refs.

681. **Air Embolism during Labour.** (Vzduchové embolie za porodu.)

By J. PRAZAK. *Ceskoslov. Gynaek.*, 12 (26), 106–109, 1947.

682. **An Analysis of Deaths from Postpartum Hemorrhage.**

By C. T. BEECHAM. *Amer. J. Obstet. Gynec.*, 53, 442–452, Mar. 1947. 7 figs.

This is a report from the Maternal Welfare Committee of the Philadelphia Medical Society. In the 15 years, 1932–1945, the maternal mortality per 10,000 fell from 7 to 2; the number of deaths from postpartum haemorrhage, however, has remained more or less constant year by year at 168 out of 529,000 births. The worst year was 1932, the sharp rise being attributed to Philadelphia's " one excursion into the realms of manual dilatation and version." It is considered that over 60 per cent of the deaths from postpartum haemorrhage could have been prevented by the doctor in charge of the case, the particular faults and omissions being tabulated thus: carelessness; inadequate care both in the antenatal period and at labour or operation; meddlesome obstetrics; poor choice of anaesthetic; mismanagement of the third stage; failure to recognize haemorrhage in time; insufficient use of oxygen, packing, and whole blood. Of the deaths, 44 per cent are attributed to simple atony of the uterus (cause unknown), 27 per cent to atony associated with placenta praevia or abruptio

placentae; and inversion was the cause in 6.5 per cent. Haemorrhage was as likely to occur after spontaneous labour as after operative delivery and general anaesthesia. Over-distension of the uterus from multiple pregnancy or hydramnios did not seem to have any particular influence.

The Committee stressed the following points in antenatal care : (1) The importance of supervising the state of general nutrition. (2) Detection of anaemic states by blood counts and haemoglobin estimation, with blood transfusion before labour in cases which do not respond to medication. (3) Routine typing of all prenatal patients. The card giving these details is kept by the patient, so that whatever hospital she may enter, time is saved if transfusion is needed. The following errors in the management of the third stage are picked out : (1) The third stage was left to an inexperienced intern or nurse. (2) Inhalation anaesthesia was continued uninterrupted through the third stage although the patient was bleeding excessively. (3) Constant palpation of the uterus or holding of the fundus was not always practised. (4) In some cases the placenta was allowed to remain in the uterus while the patient bled to death, and nothing more than suprafundal pressure was used. (5) In 11 cases inversion of the uterus with no replacement or fortifying treatment occurred. (6) After delivery of the placenta the minimum of 1 hour of close observation was not carried out. (7) Many patients bleeding abnormally after the placenta was delivered did not receive immediate packing and further measures of control; they were treated energetically only when shock was imminent.

The three major points in treatment are oxygen administration, utero-vaginal packing, and adequate blood transfusion. In Caesarean section for placenta praevia the technique advocated by Montgomery is recommended; the vagina is packed tightly before operation, and during the operation the uterus is tightly packed, the lower segment being thus held securely between the two packs. In the discussion of the paper more than one obstetrician stressed the danger of complete ether anaesthesia, believing that chloroform, given in minimal amount by one experienced in this form of anaesthesia, was much safer. The difficulty was to find an anaesthetist who had this experience.

T. C. Clare

683. Uretero Vesicovaginal Fistula of Obstetric Origin : Case Report.
By J. M. WILSON. *Urol. cutan. Rev.*, 51, 71–74, Feb. 1947. 2 figs., 2 refs.

684. Cicatricial Obliteration of the Vagina of Obstetric Origin. (Obliterações cicatriciais da vagina de origem obstétrica.)
By L. M. MACHADO. *Rev. Ginec. Obstet.*, 1, 196–200, Feb. 1947.

ANAESTHETICS, ANALGESICS

685. Analgesia and Anaesthesia in Obstetrics.
By O. S. HEYNS. *S. Afr. med. J.*, 21, 190–194, Mar. 22, 1947.

686. Demerol for Analgesia in Obstetrics.
By J. E. HALL. *Brooklyn Hosp. J.*, 5, 45–48, Jan. 1947. 2 refs.

687. Pentothal Narcosis in Gynaecology and Obstetrics. (Pentothal v gynaekologii a pôrodnictve.)
By E. DLHOS. *Ceskoslov. Gynaek.*, 12 (26), 125–136, 1947. 4 figs., 4 refs.

688. Lumbar Anaesthesia in Caesarean Sections. (Die Lumbalanästhesie bei Schnittentbindungen.)
By J. ERBSLOH and K. BRANDS. *Zbl. Gynäk.*, 69, 255–263. 1947.

689. Meningitis Following Continuous Caudal Anesthesia.
By W. W. BROWN. *Amer. J. Obstet. Gynec.*, 53, 682–683, Apr. 1947. 4 refs.

690. Preliminary Note on Peridural Anaesthesia. (Vorläufige Mitteilung über die Peridural-anästhesie.)
By K. PAULUS. *Zbl. Gynäk.*, 69, 263-266, 1947.

691. Extra-dural Anaesthesia. Use of Oleo-anaesthetics in Obstetrics and Gynaecology. (Anestesia epidurale sacrale alta. L'uso degli anestetici oleosi nel campo ostetrico e ginecologico. (Nota preventiva.)
By F. GASPAERI and T. NOBILE. *Ginecologia*, 13, 84–87, Feb. 1947.

PUERPERIUM

692. Early Ambulation in Obstetrics.
By J. E. HALL. *Brooklyn Hosp. J.*, 5, 41–44, Jan. 1947. 6 refs.

693. The Renal Threshold for Glucose in the Puerperal State. (Osservazione e considerazioni sulla soglia renale per il glucosio nello stato puerperale.)
By A. PROVENZAL. *Riv. ital. Ginec.*, 29, 281–298, 1946. 6 figs., 41 refs.

694. After-pains and their Treatment with Sodium betaglycerophosphate. (Los entuertos y su tratamiento por el beta glicerofosfato sódico.)
By L. T. SANTAMARIA. *Hisp. méd.*, 3, 481–485, Dec. 1946.

This case is reported on account of the severity of the symptoms and the success of a new form of treatment. The patient, aged 31, had previously had 4 confinements, 1 ending prematurely at 6 months. The deliveries had all been rapid, and the last one precipitate. Lactation had been satisfactory after all confinements, and the lochia scanty. Six months before the beginning of the present pregnancy an abortion occurred at 3 months com-

plicated by septicaemia. Treatment with penicillin was given, followed later by a curettage. The present pregnancy was normal, and labour terminated spontaneously with 5 intense contractions before delivery. The placenta was expelled at once with only slight loss. Within a few hours of delivery after-pains began and became severe. Twelve hours after delivery the first injection was given of 5 ml. of sodium β-glycerophosphate. [The strength of the solution and the route used for injection are not given here, but from the later part of the article it appears that a 50 per cent solution was given intravenously.] The following day the pains recurred with lactation, but the distress was relieved with a further injection of 5 ml. although the patient still noted the presence of contractions when the baby was put to the breast. The next day further pains again disappeared after a similar injection. The lochial loss was scanty. After discussing in detail the nervous and hormonal control of lactation, the author describes the use of sodium β-glycerophosphate, a drug which has been introduced into obstetrical practice in Spain, and which has been shown by graphic methods to be of value in decreasing uterine tone when excessive, in making the contractions more regular, and in prolonging the intervals between pains. Its antispasmodic action is considered to be due to the important part played by phosphorus in the metabolism of the uterine muscle. Aneurin also appears to play a part in the process. This drug is also indicated in threatened abortion, after abdominal operations in pregnancy, or when it is necessary to quieten excessive uterine action in labour. In order to avoid atonic haemorrhage it should not be given within 12 hours of delivery. An injection may be repeated after 24 hours.

[Although only a single case is reported, this new treatment of what is often a distressing condition seems to have been very successful.]

Bryan Williams

695. **The Value of the Foley Catheter in Postpartum Care.**

By W. A. RUCH. *Ural. cutan. Rev.*, 51, 75–76, Feb. 1947. 5 refs.

From a series of 1,160 deliveries 36 patients who gave evidence of infection or retention of urine in the puerperium were treated by continuous bladder drainage with a Foley catheter. Eight of these developed pyelonephritis, and were treated with sulphonamides or penicillin. It is claimed that this use of the Foley catheter combined with lavage of the bladder with boric acid solution not only adds to the patient's comfort but also reduces the incidence of postpartum cystitis and pyelonephritis.

D. M. Stern

696. **The Time for Postpartum Sterilization. Report of 150 Cases. Bacteriologic Studies on the Postpartum Uterus.**

By F. E. WHITACRE, W. M. LOEB, and L. LOEB. *Amer. J. Obstet. Gynec.*, 52, 1041–1053. Dec. 1946. 3 figs., 20 refs.

One hundred and fifty cases of postpartum sterilization by Madlencr's technique with no mortality and a morbidity rate of 9.25 per cent are recorded. Most of the patients were multiparae and 139 of the deliveries were spontaneous. The time of the operation is discussed at length. The authors advocate as the optimum time from 1 to 2 hours after spontaneous delivery. They arrive at this conclusion (1) because postpartum haemorrhage is rare after this time, and (2) from a bacteriological study of the puerperal uterus. Uterine cultures were obtained from 100 patients who had been delivered spontaneously. To determine the time of bacteriological invasion the patients were studied in groups of 10, and cultures were taken at the end of 2, 4, 6, 8, and 10 hours and at the end of the first, second, third, fourth and fifth days. Eighty-seven cultures were positive and 13 negative. The negative cultures were only obtained during the first few hours. At the end of 2 hours only 1 of 10 cultures was positive; at the end of 4 hours, 6 out of 10 cultures were positive; at the end of 6 and 8 hours, 7 out of 10 cultures were positive; at the end of 10 hours, 8 out of 10 cultures were positive; at the end of the first day 9 out of 10 cultures were positive, and from the second to the fifth day all of 40 consecutive cultures were positive.

Gladys Dodds

697. **De-Ma Therapy of Puerperal Infections.** (Die De-ma-therapie puerperaler Infektionen.)

By P. BERNHARD. *Dtsch. med. Wschr.*, 72, 66–71, Feb. 14, 1947. 7 refs.

The author defines puerperal sepsis and gives details of 50 cases. Bacteriological studies revealed a variety of organisms which could be divided into two main groups, aerobic and anaerobic. In 46 out of the 50 cases aerobic organisms were found and in 30 out of the 50 cases anaerobic organisms were seen. In only 1 case out of the 50 were anaerobic organisms alone found. Since most of the infections are mixed, it is necessary to give sulphonamide therapy in a combination effective against both aerobic and anaerobic organisms. A table is given in which the infecting organisms are divided into two groups, A, aerobic organisms, and B, anaerobic organisms. Against these two groups are given the sulphonamides which are effective in each group. "Debenal" (sulphadiazine) is effective against group A and "Marbadal" (a marfanil derivative) against group B. A combination of the two, De-Ma, should be effective in most cases of puerperal infection. A table of dosage is given, the highest dose of 10 to 13 g. in 24 hours being given in the most severe cases, so as to produce a blood concentration of 15 to 25 mg. per 100 ml. In mild cases 5 g. is sufficient, while for prophylaxis 2 to 3 g. is given locally into the uterus. In high dosage

by mouth it is advisable to give an equivalent weight of sodium bicarbonate and a glass of water with each dose. Dosage must also be correlated with body weight, the doses suggested applying to women weighing 60 kg. It is advisable to estimate the level of sulphonamide in the blood to ensure that an adequate dose is being administered. Tables show the improvement in cases of abortion, puerperal infection following childbirth, and Caesarean section as a result of the new treatment. The importance of the fight against puerperal infection and the unsurpassed results so far achieved, though only in a small number of cases, convinced the author that it was advisable to publish a preliminary survey.

Josephine Barnes

698. **A Rare Complication of Puerperal Parametritis (Osteomyelitis of the Ramus of the Pubis.)** (Uma rara complicação da parametrite puerperal. Osteomielite do ramo horizontal do pubis.)

By J. AMORIM, A. R. MARTINEZ, and J. TAVARES. *Rev. Ginec. Obstet.*, **1**, 188–194, Feb. 1947. 3 figs., 1 ref.

699. **Significance of Sulphonamides in Obstetrics and Gynaecology.** (Die Bedeutung der Sulfonamide für die Geburtshilfe und die Frauenheilkunde.)

By E. MARTIN. *Arztl. Wschr.*, **1/2**, 489–493, Feb. 28, 1947. 5 figs., 2 refs.

700. **Metabolism of Women During the Reproductive Cycle. X. The Utilization of Vitamin A During Lactation.**

By M. LESHER, J. K. BRODY, H. H. WILLIAMS, and I. G. MACY. *J. Amer. diét. Ass.*, **23**, 211–217, Mar. 1947. 20 refs.

Working in the Research Labatory, Children's Fund of Michigan, Detroit, the authors assayed the amounts of vitamin A and of carotene in the diets and in the milk of 8 nursing multiparous mothers. All received diets of similar composition in amounts to satisfy their appetite; analysis of these diets over 5-day periods showed a wide variation in the amount of the vitamin. Over this range of intake there was no effect on the amount of vitamin A secreted in the milk; the amount of the vitamin was, however, related to the volume of the milk secreted. The amount of vitamin A was small during the first 2 days postpartum, increased greatly on the third or fourth day, and then fell after the sixth day. The carotenoids were higher during the first 2 days, but also rose to a maximum on the third and fourth days, and fell after the sixth day. If it is assumed that one-fourth of the carotenoids was in the form of β-carotene, the total vitamin-A activity of the milk was 0.56 to 1.24 mg. during the first 10 days postpartum, and 0.14 to 0.64 mg. per day during periods of secretion of mature milk.

John Yudkin

THE INFANT

701. **Testing the Hearing of Newborn Infants.**

By E. FROESCHELS and H. BEEBE. *Arch. Otolaryng.*, Chicago, **44**, 710–714, Dec. 1946. 8 refs.

Although it is known that some hearing is normally present at birth the general opinion is that hearing at that time is defective, but little work has been done on infants during the first few days of life. The authors have examined 33 children between the ages of $\frac{1}{2}$ and 9 days. The most frequent reaction shown by the newborn is the acousto-palpebral (blinking) reflex. There was reaction to tuning forks by the 10 infants on whom they were used, but all except 2 responded either by blinking or, less frequently, by movements of the head or eyes to the source of sound. This is particularly interesting as it has been stated that any attempt at sound localization is a much later manifestation. The failure to respond to tuning forks may be due to the weaker intensity of the forks compared with the whistles, but it is possible that the centres for perception of pure and compound tones do not develop at the same time.

F. W. Watkyn-Thomas

702. **Children Born During the Siege of Leningrad in 1942.**

By A. N. ANTONOV. *J. Pediat.*, **30**, 250–259, Mar. 1947. 10 refs.

703. **A Case of Amelia in Healthy Foetus.** (Un caso di amelia in feto vivo e vitale.)

By U. FRASSON. *Ginecologia*, **13**, 88–95, Feb. 1947. 4 figs., 10 refs.

704. **Acardiacs and Hemicardiacs.** (Acardios—hemicardios.)

By O. A. ITOIZ and L. A. GUERRA. *Obstet. Ginec. lat.-amer.*, **4**, 912–919, Dec. 31, 1946. 6 figs.

705. **Twin Monsters : Comments on Two Clinical Cases.** (Monstruos Dobles : Comentarios a dos casos clínicos.)

By J. L. Oliva. *Toko-ginec. pract.*, **6**, 128–137, Apr. 1947. 5 figs.

706. **Premature Infants.** (Les prématurés.)

By B. FORTIER and P. LADOUCEUR-DUPUIS. *Union méd. Can.*, **76**, 263–268, Mar. 1947. 3 figs.

707. **Tetanus of the Newborn and Uterine Tetanus.** (Tétanos del recién nacido (tétanos neonatorum) y tétanos uterino.)

By M. PENSADO. *Toko-ginec. práct.*, **6**, 117–124, Apr. 1947. 2 figs.

708. **The Blood in Infancy.**

By L. FINDLAY. *Arch. Dis. Childh.*, **21**, 195–208, Dec., 1946. 20 figs., 13 refs.

The author, working at the Radcliffe Infirmary, Oxford, analyses observations made both on foetal blood, obtained from the cord immediately after

delivery, and on blood taken at intervals throughout the first year of life, from a number of premature and normal babies. His results are of considerable interest. He found that both haemoglobin and red cells increase rapidly in the first few hours after delivery, being higher in the newborn child a few hours old than in the foetus. The fall that occurs in red cells and haemoglobin during the first days of life he attributes to a lag in production rather than to increased cell destruction. Evidence in favour of this hypothesis is given, but while claiming that icterus neonatorum is unrelated to the degree of haemolysis present he gives no other explanation of the cause of this jaundice. He found that the fall in red cells and in haemoglobin is not exactly parallel, nor is it associated with changes in cell size, which is smaller during the postnatal than during antenatal life. The total fall in red cells and haemoglobin, based on calculation from body weight and not on direct observation, is described as less than the percentage fall. The administration of iron to both healthy and premature babies causes an immediate but only temporary rise in haemoglobin and red cells. It is therefore concluded that iron causes a temporary irritation of haemopoietic tissue only, and that its long-term therapeutic effects, claimed particularly by Mackay, are not proven.

[Interested workers are advised to consult the original paper, since the conclusions and results of the author differ in some important respects from those of previous workers.]

Janet Vaughan

709. Parenteral Vitamin K Therapy during the Ante-partum Period and its Effects on the Infant's Prothrombin Levels.

By C. REICH, R. L. McCREADY, and H. CHAPLIN. *Amer. J. Obstet. Gynec.*, **53**, 300–302, Feb. 1947. 1 fig., 8 refs.

In 1941 McCready *et al.* published (*Amer. J. Obstet. Gynec.*, **42**, 398) a preliminary report on the effectiveness of injections of vitamin K administered to the mother at the onset of or during labour in reducing the mortality from haemorrhagic disease of the newborn. They found that the prothrombin level of the maternal blood was unaffected, that there was a definite rise in the prothrombin level of the infant, and that this elevation occurred quickly following injection. These studies have now been extended to a further series of 500 cases.

Twenty mg. of menadione bisulphite or "hykinone" was injected into the mother during labour. If the latter was prolonged this injection was repeated. Prothrombin estimations were made on the infant daily for the first week. The prothrombin was prepared by Shapiro's method, 100 mg. being mixed with 5 ml. of saline and inactivated at 58° C. for 15 minutes. Twenty c.mm. of blood were taken from the infant's heel

and blown from a Sahli pipette into the prothrombin solution. Of the treated infants, 99 per cent had a normal prothrombin time from the first day. Where no vitamin K was given, prothrombin times in the infant started at 45 seconds on the first day, rose to 60 seconds from the second to the fourth day, and dropped to a normal of 32 seconds on the seventh day. The authors again stress the value of this therapy in preventing all manifestations of haemorrhagic disease of the newborn.

Kenneth Bowes

710. Heterospecific Pregnancy : I. The Clinical Importance of the Rh Factor.

By P. M. DE BURGH, R. A. SANGER, and R. J. WALSH. *Med. J. Aust.*, **1**, 174–176, Feb. 8, 1947. 4 refs.

The authors report the results of tests for Rh antibody in the serum of 54 mothers who had children suspected to be suffering from haemolytic disease. In all but 7 either anti-Rh agglutinin or incomplete antibody (more often the latter) was found. [In 5 of the 7 the accompanying history does not look like that of haemolytic disease. Since all the mothers included were Rh-negative, there must have been 30 or so similar cases where the mother was Rh-positive; these have not been reported.] The authors conclude that " haemolytic disease in the infant is almost always associated with detectable evidence of iso-immunization when the disease is due to Rh incompatibility as the cause of foetal or neonatal disorder."

R. R. Race

711. The Treatment of Erythroblastosis Foetalis.

By I. A. B. CATHIE. *Arch. Dis. Childh.*, **21**, 229–234, Dec. 1946. 2 figs., 11 refs.

From an experience of 38 cases of erythroblastosis foetalis in the Hospital for Sick Children, Great Ormond Street, London, the author has formed certain impressions of the value of various methods of transfusion therapy. He advocates an initial transfusion of up to 200 ml. of Rh-negative blood, given by cannula at the rate of 15 to 20 ml. an hour. Thereafter he is in favour of smaller transfusions of 60 to 80 ml. given by scalp vein so that the treatment can be carried on without keeping the infant in hospital. He does not advocate raising the red cell count of affected infants as high as 5,000,000 per c.mm., stating that above a level of 3 to 3½ million per c.mm., the peripheral red cells lyse and return to their individual level. In one case an infant received 750 ml. of Rh-negative blood in 5 weeks and yet had a red cell count of only 4,200,000 per c.mm. at the end of it. The author considers that this is a certain proof of an increased rate of destruction of Rh-negative cells; since in the absence of lysis a count of 12,000,000 per c.mm. would have been expected.

Two pieces of experimental work are discussed. (1) Ten consecutive affected infants were tested at

weekly intervals by the anti-human-globulin test of Coombs, Mourant, and Race, which detects sensitization of the infant's red cells by (anti-Rh) antibodies. All were sensitized on admission and some were sensitized at the end of 3 weeks. By the fourth week only 1 was still sensitized. (2) Experiments were made in which high-titre Rh antibody was given by mouth, and in no case was antibody demonstrable in the blood thereafter, either by direct or by sensitization tests.

[This statement is unsupported by any details, such as the ages of the recipients, the quantity of antibody consumed, the titre of the antibodies, or the Rh groups of the recipients; in the absence of this information the reader is quite unable to judge the value of the observations. On the question of transfusion therapy it is difficult to form an opinion from the data provided. For instance, since details on only one case are given, one would like to know the red cell count of the citrated blood used, for how long the blood used had been stored, to what level the red cell count rose after each transfusion, and so forth. Because of the difficulty of drawing conclusions about the survival time of transfused erythrocytes from observations on changes in the recipient's total red cell count, other workers have studied directly the survival rate of Rh-negative and Rh-positive cells. Such studies have shown that, with few exceptions, Rh-negative cells circulating in an infant affected with haemolytic disease are not subject to a materially greater rate of destruction than are normal cells circulating in a normal adult, even when the infant's red cell count is raised to 6,000,000 per c.mm. These observations lend no support to the idea that any regular increase in the rate of destruction occurs when the infant's total red cell count exceeds a certain figure. The author makes no detailed examination of this published work, and his evidence must be considered inadequate to refute it.]

P. L. Mollison

712. **Substitution Transfusion : A New Treatment for Severe Erythroblastosis Fetalis.**

By H. WALLERSTEIN. *Amer. J. Dis. Child.*, **73**, 19–33, Jan. 1947. 46 refs.

A method is described of substitution transfusion given immediately after birth in the sub-icteric stage of haemolytic disease of the newborn to prevent subsequent damage to the liver and brain. Hepatic damage in cases of icterus gravis by excessive red-cell haemolysis and a reactive liver haemopoiesis has been recognized. If this is to be avoided the end-products of haemolysis must be removed or their formation prevented. This may be done by withdrawal of the infant's Rh-positive cells and their replacement by harmless Rh-negative cells. Withdrawal and replacement should be carried out simultaneously. The technique is as follows : (1) Isotonic saline or pooled plasma is infused into an arm vein. (2) Blood (56 to 60 ml.) is withdrawn by syringe from the longitudinal sinus. (3) Rh-negative blood of a compatible group replaces the plasma or saline infusion. (4) When an estimated substitution of 80 per cent has been accomplished the needle is removed from the fontanelle. The estimate is based on the infant's weight, counting the total blood volume as 10 per cent. (5) The infusion is continued until 75 to 100 ml. of Rh-negative blood has been given in excess of the amount recovered, 10 ml. of 10 per cent calcium gluconate being injected into the vein to counteract the citrate in the blood or plasma. The procedure takes from ½ to 1½ hours. Alternatively blood may be withdrawn from a small branch of the radial artery at the wrist. It is difficult to obtain enough blood from superficial veins. [Withdrawal of blood from the longitudinal sinus is not without its dangers in a jaundiced baby.]

Details of cases are given in all of which the prognosis was considered grave. Seven patients recovered and 2 died, both of whom might have recovered if treatment could have been started in the first 24 hours of life. Emphasis on the anaemia as the indication for treatment is an error; the protection of the liver is the primary indication. About 30 per cent of cases of haemolytic disease show liver damage and 10 per cent kernicterus; until these changes can be accurately forecast substitution transfusion should be used in all cases. If cases are to be selected the following are the most helpful criteria : (1) multiparity with a history of erythroblastis in previous pregnancies; (2) serological studies; (3) during delivery, the presence of icteric amniotic fluid; (4) and excessively large pale placenta; (5) excess of nucleated red cells in the blood in the cord. With such indications, preparations should be made in advance and substitution therapy instituted as soon as the baby is born.

A. G. Watkins

713. **Infant Feeding.**

By M. D. BLACK. *J. Obstet. Gynaec., Lahore*, **8**, 47–50, Apr. 1947.

714. **Neonatal Mortality and its Causes.** (Neonatale sterfte en haar oorzaken.)

By F. WILLEMIJNS. *Belg. Tijdschr. Geneesk.*, **3**, 346–352, Apr. 1947. 3 refs.

715. **Prevention of Fetal Wastage.**

By L. V. DILL and J. W. PEARSON. *Surg. Clin. N. Amer.*, **27**, 453–460, Apr. 1947. 14 refs.

716. **Rates of Stillbirths in Canada.**

By H. L. ROBINSON. *Canad. J. publ. Hlth.*, **38**, 168–181. Apr. 1947. 7 figs.

See also Nos. 607, 608, 635.

MATERNAL MORTALITY

717. Maternal Mortality During the War Years in Omsk.

By B. Z. VICKER. *Akush. Ginek.*, 1, 36–40, 1947.

718. Maternal Mortality in Brooklyn for 1945.

By C. A. GORDON. *N. Y. St. J. Med.*, 47, 595–599. Mar. 15, 1947. 5 figs.

719. Sudden Death during Pregnancy, Labour and Confinement. (Ein Beitrag zum plötzlichen Tod in der Schwangerschaft unter der Geburt und im Wochenbett.)

By O. H. MOELL. *Zbl. Gynäk.*, 69, 266–275, 1947. 32 refs.

OBSTETRIC OPERATIONS

720. The Prognosis of Caesarean Section in Relation to the Degree of Infection of the Birth Canal in Cases of Pelvic Dystocia. (La prognosi del taglio cesareo in rapporto al grado di purezza delle vie genitali nei casi di distocia pelvica.)

By M. CARBONINI. *Ginecologia, Torino*, 13, 107–144, Mar. 1947. 2 figs., 28 refs.

721. Caesarean Section : Successful Operation in a Case of Spontaneous Complete Rupture and another of Imminent Rupture of the Uterus. (El parto en las cesareadas. Un caso de rotura completa silenciosa y otro de rotura inminente de útero después de cesáreas, operados con éxito.)

By C. FERNANDEZ-RUIZ. *Clin. y Lab.*, 43, 276–280, Apr. 1947. 9 refs.

722. Abdominal Drainage after Caesarean Section in Infected Cases. (El drenaje abdominal en la operación cesárea del caso impuro.)

By A. PERALTA RAMOS. *Prensa méd. argent.*, 34, 343–349, Feb. 21, 1947.

723. Critical Study of Caesarean Section. (Estudo crítico da cesária.)

By B. P. M. TOLOSA and J. ONOFRE ARAUJO. *An. brasil. Ginec.*, 22, 370–383, Nov. 1946. 19 refs.

724. Late Caesarean Section in Foetal Monstrosity in Twin Pregnancy complicated by Hydramnios. (Taglio cesareo ritardato per mostruosità fetale in gravidanza gemellare complicata da idramnios.)

By R. FLAMINIO DONDI. *Arch. Ostet. Ginec.*, 51, 349–356, Nov.–Dec. 1946. 4 figs.

725. Prophylactic Intraperitoneal Sulphanilamide in the Obstetric Surgery of the Infected Case. (La sulfanilamida intraperitoneal profiláctica en la cirugía obstétrica del caso impuro.)

By M. L. PEREZ. *Rev. esp. Obstet. Ginec.*, 5, 360–372, Dec. 1946. Bibliography.

MISCELLANEOUS

726. The Organization of Obstetrics in Sweden. (L'organisation de l'obstétrique en Suède.)

By A. SJOVALL and G. T. HEDBERG. *Gynéc. Obstét.*, 46, 32–36, 1947. 1 fig.

727. The Regional Organization of Obstetrics in France. (L'organisation regionale de l'obstétrique en France.)

By P. LANTUEJOUL, E. CHOME, and R. MERGER. *Gynéc. Obstét.*, 45, 738–755, 1946.

728. The Role of the General Practitioner in Future Midwifery Practice.

By J. B. DEWAR. *Edinb. med. J.*, 54, 228–238, Apr.–May, 1947.

729. Psychical Conditions in Woman in Relation to the Processes of Procreation. (Estados psiquicos de la mujer en relación con los procesos de la generación.)

By D. E. PARACHE GUILLEN. *Toko-ginec. Práct.*, 6, 1–34, Jan.–Feb. 1947.

730. Effect of War on Pregnancy. (Kriegseinflüsse auf die Schwangerschaft. Ein statistischer Beitrag.)

By A. HUBER. *Klin. Med., Wien.*, 2, 49–65, Jan. 15, 1947. 1 fig., 61 refs.

GYNAECOLOGY

731. Ectopic Kidney and Gynaecological Affections. (Ectopias renales y ginecopatías.)

By J. M. SALA PONSATI. *Rev. esp. Obstet. Ginec.*, 6, 20–24, Jan.–Feb. 1947.

732. Relief of Pelvic Pain by Sympathectomy and Intraspinal Alcohol Injections.

By J. P. GREENHILL. *J. int. Col. Surg.*, 10, 218–222, Mar.–Apr. 1947. 10 refs.

733. The Local Action of Female Sex Hormones. (Über die lokale Wirkung der weiblichen Genitalhormone.)

By H. RUNGE. *Dtsch. med. Wschr.*, 72, 25–28, Jan. 17, 1947. 1 fig., 1 ref.

Female sex hormones, like the hormones of other internal secretory glands, are set free into the general circulation and act on special tissues. This indirect route of action does not preclude the possibility that other more direct routes exist. Siegert, Gumbrecht, and Löser have suggested that liquor folliculi is discharged into the Fallopian tube along with the ovum, and may have a direct action on the endometrium and on the Fallopian tube. This theory is probably incorrect, as the menstrual cycle is rarely disturbed when the tubes are blocked. Liquor folliculi may also pass through the large network of lymphatics in the mesovarium.

The author considers pregnancy a favourable time for investigating the local action of female sex hormones. It is well known that removal of the ovary containing the corpus luteum of pregnancy

is not followed by abortion. The chorion is the source of the necessary hormones for the continuation of pregnancy; as the chorion lies in close contact with the uterine wall local action of the hormones on the wall is likely to take place. Arbogast, assistant to Runge, has investigated this point. He sectioned and measured the length of muscle fibres of a non-pregnant uterus, a uterus 8 weeks after conception, and another 10 weeks after conception. The muscle fibres in the non-pregnant uterus were of practically the same length all over the organ, while in the 8-weeks pregnant uterus the muscle fibres were considerably larger and longer in the wall where the ovum was implanted than in the opposite wall. In the 10-weeks pregnant uterus the muscle fibres were large throughout the organ. The author suggests that the increase in size of the muscle fibres is brought about by the local action of the high concentration of hormones produced in the chorion.

Further investigations made by another assistant, Hoff, are described. These researches concern the dilatation, hypertrophy, and loss of motility in the ureter in pregnancy. Hoff inserted a catheter through the kidney substance into the pelvis of the kidney of dogs, washed various solutions through the ureter, passed radio-opaque substances into the ureter, and observed the effect radiologically. Urine from pregnant dogs introduced through the catheter into the ureter produced the typical pregnancy changes. Human urine and Ringer's solution had no effect. Heated pregnancy urine had the same effect as untreated pregnancy urine, although heating destroyed the gonadotrophic hormones. A solution of follicular hormone produced changes unlike those caused by pregnancy. Corpus luteum hormone (25 mg. " proluton ") was next injected intramuscularly; changes similar to those of pregnancy were seen. To decide whether the changes were produced by corpus luteum hormone locally, unilateral nephrectomy was performed. On the nephrectomized side slight changes were seen in the ureter, while on the other side typical pregnancy changes occurred. Proluton is excreted in the urine as pregnandiol, and this substance is generally regarded as being inert. These investigations suggest, however, that it still possesses sufficient activity to cause changes in the ureter with which it is in contact.

Runge has therefore demonstrated that the female sex hormones have a local action on the uterus and the ureters.

Gladys Dodds

734. Depot Effect of Oestrogens in Aqueous Solution. Pervaginal Hormonal Treatment. (Zur Depotwirkung oestrogener Stoffe in wasseriger Lösung. Zugleich ein Beitrag über pervaginal Hormonbehandlung.)

By E. PREISSECKER. *Klin. Med., Wien.*, **2**, 135–138, Feb. 1, 1947. 7 refs.

735. Experience with the Therapeutic Use of Oestrogenic Agents in the Form of Crystals. (Erfahrungen mit der therapeutischen Anwendung oestrogener Wirkstoffe in Kristallform.)

By K. J. ANSELMINO and H. R. SCHILDBACH. *Dtsch. med. Wschr.*, **72**, 179–183, Apr. 18, 1947. 1 fig. 29 refs.

736. Our Experience with Oestrogen Pellet Implantation. (Nuestra experiencia en la inclusión de estrógenos.)

By A. ACHARD. *An. brasil. Ginec.*, **23**, 4–15, Jan. 1947.

Disorders of Function.

737. Hormone Therapy in Relation to the Menstrual Cycle. (Hormonoterapia en relacion con el ciclo menstrual.)

By G. ZENTENO. *Rev. méd. Hosp. gen.*, **9**, 337–354, Feb. 1947. 6 figs.

738. Vaginal Smears in Ovarian Dysfunction. (Les frottis dans les dysfonctions ovariennes.)

By A. LICHTWITZ and M. FITOUSSI. *Sem. Hôp. Paris*, **23**, 695–700, Mar. 21, 1947. 2 figs., 19 refs.

In order to interpret correctly a patient's vaginal smear, it is necessary not only to be familiar with the appearances of the cells during the different phases of a normal cycle, but also to obtain a succession of smears, taken not less frequently than every 3 days, throughout a whole cycle. The smears may contain evidence of atrophy (either complete or " subatrophy ") or of *hypersecretion of folliculin*. Completely atrophic smears contain chiefly small basophil cells with large nuclei, and occasional navicular cells; " subatrophic " smears consist chiefly of large polygonal basophil cells with large nuclei, and a few polygonal basophil cells with small pyknotic nuclei. These types of smear are found before puberty and often (though not invariably) after the menopause, in ovarian insufficiency (whether primary or secondary), in Simmond's disease, in Fröhlich's syndrome, in acromegaly, in pituitary or ovarian types of dwarfism, in all amenorrhoeas (whatever the original cause), in Cushing's syndrome, in the presence of adrenal tumours, in myxoedema, in some cases of hirsutism and of hyperthyroidism, in ovarian or uterine hypoplasia (including infantile uterus), in uterine infections and tumours, and finally when pituitary secretion is deficient. Smears indicating hypersecretion of folliculin contain chiefly keratinized eosinophil cells, which do not show regressive characteristics in the post-ovular and the pre-menstrual phases (this usually indicating absence of ovulation). This type of smear is generally found associated with granulosa-cell tumours, ovarian cysts, simultaneous development of more than one Graafian follicle, infections of the cervix or of the Fallopian tubes, hepatitis, cirrhosis of the liver, and several

rare conditions of obscure pathology, such as idiopathic variation in the renal threshold for oestrogens.

· *Nicolas Tereshchenko*

739. Vaginal Smears. The Oestrogen influenced Cell Picture in Amenorrhoea. Irregularity of Menses. Uterine Haemorrhages. (Le film de l'oestrogenie cellulaire dans l'amenorrhée. Les règles irrégulières. Les hémorragies uterines.)

By A. Lichtwitz and M. Fitoussi *Sem. Hôp. Paris*, 23, 701–708, Mar. 21, 1947. 7 figs., 38 refs.

The examination of a single isolated vaginal smear is not superior in value to any of the other methods of estimating ovarian activity, such as an endometrial biopsy, but the successive variations in activity during a menstrual cycle can best be studied by means of vaginal smears, even in the presence of infection. In every smear the following points must be carefully noted: (1) the dimensions and shape of the cells and their staining reactions; (2) the dimensions of the nuclei and their structural details; (3) the disposition of the cells, whether discrete and separated or adherent to each other; (4) the presence or absence of associated extraneous elements: (a) mucus; (b) leucocytes; (c) red blood cells; and (d) organisms and debris. In amenorrhoea the smears remain of the same type throughout the cycle, but in different cases may either be atrophic or " subatrophic " in character or show evidence of moderate folliculin lack or of hypersection of folliculin. When the smear is atrophic or " subatrophic " the amenorrhoea may be due to a primary pituitary insufficiency with normal ovaries, or to a primary ovarian insufficiency. The treatment consists in re-establishing a normal cycle through the administration of the appropriate hormone during the appropriate phase· of the cycle; the dosage and the effect of the treatment are determined and checked by frequent and repeated examinations of vaginal smears. If hypersecretion of folliculin is the cause of the amenorrhoea the treatment consists of the administration of androgens during the first half of the cycle, followed by the administration of lutein during the second half. In menstrual irregularities the vaginal smear may indicate either excessive folliculin secretion or insufficient folliculin secretion. The type of smear and the phase of the menstrual cycle when the excess or the deficiency manifests itself indicate the correct treatment, the dosage being regulated and the effect of the treatment closely followed by the examination of vaginal smears. In uterine haemorrhages again vaginal smears may indicate either excess or deficiency of folliculin. The excess may occur either before or after ovulation; in the first case the treatment consists of the administration of androgens during the first half of the cycle; in the second type of case the treatment consists in the administration of lutein during the second half of the cycle;

the effect is observed in the usual way by means of repeated vaginal smears.

This valuable article concludes with a summary of the various types of patients in whom the use of vaginal smears is an easily performed and helpful adjunct to correct diagnosis and treatment.

Nicolas Tereshchenko

740. The Treatment of Amenorrhea in Young Women.

By L. M. Randall. *Amer. J. Obstet. Gynec.*, 53, 453–458, Mar. 1947. 1 ref.

This paper, from the Section of Obstetrics and Gynaecology, Mayo Clinic, deals with the procedures employed in the treatment of a group of 87 young women with amenorrhoea of 1 to 4 years' duration. Cases where tumours were found ·are excluded. The nutritional state is important and is first investigated. Patients suffering from anorexia nervosa or functional anorexia are given a balanced ration rich in proteins and vitamins. An estimate of the calorie intake is made, and to this amount 300 calories is added daily. After 5 or 6 days a further 300 calories is added, this procedure being continued until the intake is about 3,500 calories, after which the basal metabolic rate returns to normal and weight increases. Cyclic administration of oestrogens may then be started in an attempt to shorten ·the period of uterine atrophy usually occurring in these cases. When examination of the endometrium reveals hypoplasia it is advisable to begin cyclic administration of oestrogens for 2 or 3 weeks in every 4. Diethylstilboestrol is generally used, given to the limit of tolerance. This form of treatment stimulates the uterus and endometrium and indirectly the pituitary body. By the addition of progesterone a more complete stimulation may be achieved.

Thyroid extract is generally recognized as efficacious in the treatment of amenorrhoea in properly selected cases. It is important to determine the basal metabolic rate (B.M.R.) before beginning treatment. If the B.M.R. is − 15 to − 20 per cent the patient is given 3 or 4 gr. (0.02 to 0.25 g.) of desiccated thyroid substance daily for 3 days, 2 gr. (0.13 g.) for 3 days, and then 1 to 1½ gr. (0.065 to 0.1 g.) daily. The B.M.R. is again estimated after the first week, after which it is usually possible to determine the maintenance dose, which may have to be continued indefinitely. Estimation of the B.M.R. from time to time is advisable. In the presence of a lowered B.M.R. other forms of substitutional treatment are ineffective. In some cases thyroid extract is the only treatment necessary.

X-ray irradiation in small doses to the pituitary or ovaries, or both, has been used safely and effectively at the Mayo Clinic for eighteen years. Such treatment is often successful in re-establishing the menses, but the effect is frequently only temporary and treatment has to be repeated. It is

more successful in cases where amenorrhoea is due to pituitary failure. Extrinsic gonadotrophins, though they have a place in the treatment of amenorrhoea, were little used in 'this series.

In 17 of the 87 patients there was ovarian dysfunction; in 36 there was evidence of pituitary failure; 26 responded to treatment. Fifteen had anorexia nervosa; 8 were cured. Nineteen had primary amenorrhoea; in 3 of these menstruation started after treatment.

T. C. Clarc

741. X-ray Irradiation to Promote Ovulation.

By J. O. HAMAN. *West. J. Surg.*, 55, 107–113, Feb. 1947. 3 figs., 10 refs.

Since the introduction of X-ray irradiation of pituitary and ovaries to treat secondary amenorrhoea by van de Velde in 1914 enthusiastic advocacy of the method has vied with hearty condemnation. The main objections were: (1) possible harm, such as production of permanent amenorrhoea; (2) production in many animals of abnormalities in the second and third generations by X-ray treatment. A search of the literature has not disclosed harm to patient or offspring from properly used low-voltage irradiation. The author therefore contends that the above objections are speculative.

Treatment should be preceded by pelvic examination and a pregnancy diagnosis test unless the patient has menstruated in the preceding 2 weeks. Basal body temperature records should show lack of ovulation. The mechanism of the therapy is not understood. No cytological changes have been shown in the ovary or pituitary. The first eleven cases treated by the author received X-rays by the Edeiken technique—that is, 135 kV, 5 mA, at 40 cm. distance with 6 mm. of aluminium filtration through an anterior pelvic field of 20 × 20 cm., a similar dosage being given to the pituitary simultaneously through a portal of 3 × 3 cm. The remaining patients were treated alternately with a slight modification.

Treatment resulted in restoration of normal menstruation, as shown by basal body temperature curves and/or biopsy in 71 per cent of 32 cases of secondary amenorrhoea. The percentage of cures was inversely proportional to the length of amenorrhoea, the average in the series being 6 months. Pregnancy followed in 12 women out of 18 who complained of sterility and amenorrhoea; all the offspring were normal. The author concludes that X-ray irradiation appears to be the most effective and economical treatment of secondary amenorrhoea with its accompanying sterility.

In the discussion of the paper Rubin reported similar experiences of his own and of Kaplan. Oligomenorrhoea and amenorrhoea suggested lowered fertility, and statistical study of 1,000 cases with these symptoms showed 4 to 6 per cent of spontaneous pregnancies. He stressed the importance of ensuring that the patient was not pregnant before treatment, and stated that irradiation of a pregnant uterus in the early weeks of gestation results in production of a monstrosity in 90 per cent of cases. He quoted the work of Frank on some 150 to 200 cases in which he used X-ray therapy to induce abortion, in every case with a successful result.

C. W. Kimbell

742. Amenorrhea not associated with Pregnancy in Young Women.

By L. M. RANDALL. *Amer. J. Obstet. Gynec.*, 52, 975–983, Dec. 1946. 5 refs.

This paper is based on data obtained during an investigation of 94 women between the ages of 19 and 25 who had not menstruated for 1 year or longer. Cases in which amenorrhoea was associated with organic disease and physiological disturbances of the glands primarily concerned with menstruation were excluded. Of the 5 groups, the first comprised 19 patients in whom menstruation had not occurred by the age of 19 years. Development anomalies of the vagina and congenital hypoplasia of the uterus, with or without under-development of the' secondary sex characters, accounted for most cases in the group.

Amenorrhoea associated with tumours is comparatively rare, and there were only 7 cases in the series. Four of the tumours were located in the pituitary; one was a glioma in the floor of the fourth ventricle, and 2 were in the adrenal gland. The author considers that chromophobe tumours of the pituitary and suprasellar lesions are often relatively silent, and that a thorough radiological examination of the sella turcica in all patients with amenorrhoea is therefore necessary.

In the third group there were 15 patients in whom amenorrhoea was associated with anorexia nervosa. In the author's experience approximately 50 per cent of young women suffering from anorexia nervosa also have amenorrhoea. There is a tendency to confuse the findings in these patients with those in pituitary cachexia and Simmons's disease. However, Sheehan (*Quart. J. Med.*, 1939, 8, 277) has pointed out that the destructive lesion of the pituitary in Simmonds's disease most frequently occurs as a result of shock and haemorrhage at the time of delivery and that confusion arises from the misconception that patients who have Simmonds's disease usually show cachexia.

In group 4 there were 17 women who suffered from secondary amenorrhoea, which, in the author's view, resulted from a failure of ovarian function. Each had cyclical symptoms of nervous tension, menstrual molimina, or vasomotor upsets without flow. Physical examination of these patients revealed nothing characteristic, and there was no constant finding, but 70 per cent gave a history of previous menstrual abnormality. The last group, the largest, comprised 36 patients who had secondary amenorrhoea associated with failure

of gonadotrophic secretion of the anterior lobe of the hypophysis. These patients had no cyclic symptoms, and only 36 per cent gave a history of previous menstrual irregularities as compared with 70 per cent of the previous group. As a general rule, the uterus in these cases was considerably reduced in size and the endometrium atrophic.

The author emphasizes that amenorrhoea is a symptom and not a disease. A careful investigation of patients with amenorrhoea is necessary, special attention being paid to the history, physical examination, and radiograph of the pituitary fossa. Laboratory examination for disturbances of endocrine function is of doubtful value and often leaves the physician without an explanation of the amenorrhoea.   *R. L. Hartley*

743. Psychogenic or " Hypothalamic " Amenorrhea. By E. C. REIFENSTEIN. *Med. Clin. N. Amer.*, **30**, 1103–1114, Sept. 1946. 2 figs., 8 refs.

The author draws attention to disturbances in the hypothalamus as a cause of amenorrhoea. The sequence of events in the normal menstrual cycle is reviewed and is now believed to depend on a balance between the anterior pituitary follicle-stimulating and luteinizing hormones and the ovarian hormones, oestradiol and progesterone. Amenorrhoea will result if the anterior pituitary or ovary are not producing their hormones or if the endometrium is absent or fails to respond to hormone stimuli. A simple test for estimating follicle-stimulating hormone in the urine is now available, while oestrogen production may be measured in various ways.

The hormonal pattern in the condition which the author calls " hypothalamic amenorrhoea " is described. There is normal secretion of follicle-stimulating hormone but oestrogen is absent and the endometrium and vaginal mucosa are atrophic. No bleeding follows administration of progesterone but the endometrium is capable of responding to oestrogens. When the case histories of these patients were reviewed it was found that many had detectable psychogenic factors. The author suggests that the mechanism is a loss of nerve impulses from the hypothalamus, so that the anterior pituitary does not release its luteinizing hormone. Diagnosis depends on a history of psychic trauma preceding the period of amenorrhoea. Follicle-stimulating hormone is excreted in normal amounts. Oestrogens are absent and there is no response to progesterone. Oestrogens will produce withdrawal bleeding. There may be a slight decrease in excretion of 17-ketosteroids. Exposure to radium or X-rays or recent infection must be eliminated as a cause of the amenorrhoea.

Treatment consists of explanation and, if necessary, psychotherapy. Substitution therapy with ovarian or pituitary hormones may be tried and small doses of thyroid are sometimes effective. Good results have been obtained by the continued administration for some months of a small dose, 0.1 mg., of diethylstilboestrol daily. It is suggested that this stimulates the pituitary to produce luteinizing hormones. Evidence is offered to show that the release of luteinizing hormone from the anterior pituitary is brought about by impulses passing along the hypothalamo-pituitary nerve pathway, and that the presence of luteinizing hormone is necessary for oestrogen production. Detailed case records from 2 patients are given.

[The importance of psychogenic disturbance in causing amenorrhoea, especially in young women, is well known. The explanation offered by the author, though highly conjectural, may be the correct one, but two criticisms are offered. First, the causation of amenorrhoea by organic disease, notably tuberculosis, is overlooked. Secondly, the role of the thyroid gland, probably of some importance in these cases, is not mentioned, though the author does note that some cases benefited from small doses of thyroid. Caution must be exercised in claiming cure from any one measure in a condition where spontaneous recovery in a matter of a few months is a well-known occurrence.]

Josephine Barnes

744. Amenorrhoea at the Terezin Concentration Camp. (L'amenorrhee au camp de concentration de Terezin (Theresienstadt).)
By F. BASS. *Gynaecologia, Basel*, **123**, 211–219, Apr. 1947. 2 figs.

745. Investigations into the Uterine Mucosa. IV. Pathological and Clinical Classification of Metropathia Haemorrhagica. [In English]
By B. FALCONER. *Acta. obstet. gynec. scand.*, **27**, Suppl. 5, 1–101, 1947. 12 figs., bibliography.

746. A Preliminary Evaluation of Dienestrol in the Menopause.
By R. FINKLER and S. BECKER. *Amer. J. Obstet. Gynec.*, **53**, 513–519, Mar. 1947. 4 figs., 14 refs.

Dienoestrol in doses of from 0.2 to 1.5 mg. daily was administered to 73 patients who complained of menopausal symptoms. The majority of these women (58.9 per cent) had undergone a spontaneous menopause; in others it had followed hysterectomy, castration, or irradiation. Dosage was assessed by the relief of symptoms, and was checked by vaginal smear. Symptoms were relieved in 99.5 per cent. The remainder of the patients were suffering, in addition, from intercurrent disease (mental depression, alopecia areata, or psychoneurosis). Some patients had previously received other oestrogenic therapy without benefit. Only 2 of them suffered from withdrawal bleeding, and in both it was mild. Three patients complained of nausea. After initial relief of symptoms the maintenance dose of 0.3 mg. was usually sufficient —the drug being gradually discontinued later.

D. M. Stern

747. Climacteric.

By B. L. KAPUR. *J. Obstet. Gynaec., Lahore*, 8, 24–28 Feb. 1947. 32 refs.

748. Management of the Menopause and Climacteric.

By W. P. BEVEREUX. *Texas St. J. Med.*, 42, 683–687, Apr. 1947. 12 refs.

749. Menopausal Haemorrhage. (Ueber Blutungen in der Menopause.)

By H. L. KOTTMEIER. *Acta obstet. ginec. scand.*, 27, Suppl. 6, 1–227, 1947. 28 figs., bibliography.

750. Review of 422 Cases of " Sterility " in Private Practice.

By A. C. FROST and H. C. G. FROST. *Bull. Vancouver med. Ass.* 23, 103–109, Feb. 1947. 12 refs.

751. Female Sterility of Tubal Origin without Anatomical Lesion. (Stérilité féminine d'origine tubaire sans lésion anatomique.)

By J. KREIS. *Rev. franç. Gynéc.*, 42, 55–58, Feb. 1947.

752. Bilateral Occlusion of the Oviducts as a Cause of Sterility in Spain. (La oclusion bilateral de los oviductos como causa de esterilidad en nuestro medio.)

By A. CLAVERO NUNEZ. *Rev. esp. Obstet. Ginec.*, 5, 342–343, Dec. 1946. 5 refs.

753. Investigation and Treatment of Infertility.

By S. H. STURGIS. *Bull. New Engl. med. Center*, 9, 49–54, Apr. 1947.

754. The Dangers of the Intracervical Pessary as a Contraceptive Device.

By S. L. ISRAEL and D. G. HARREL. *Amer. J. Obstet. Gynec.*, 53, 684–687, Apr. 1947. 1 fig.

Abnormalities of the Reproductive Organs.

755. Malformation of the Genito-urinary Organs. (Malformação dos orgaos genito-urinários.)

By J. POGGI. *Rev. Ginéc. Obstét.*, 11, 345–364, Dec. 1946. 6 figs., 28 refs.

756. Complete Absence of the Vagina; Successful Treatment by Autotransplantation of the Intestine. (Ausencia completa de la vagina. Tratada con autotransplantación del intestino. Curación.)

By M. J. LUQUE. *Rev. brasil. Cir.*, 16, 143–152, Mar. 1947. 10 figs.

757. A Rare Case of Uterine Malformation.

By J. E. R. HEPPOLETTE. *J. Obstet. Gynaec., Lahore*, 8, 15–23, Feb., 1947. 2 figs.

758. A Rare Congenital Anomaly: True Uterus Unicornis and Unilateral Renal Agenesis. (Une anomalie congenitale rare. Utérus unicorne vrai et agénésie rénale unilatérale.)

By M. FRILEUX. *Gynécologie*, 44, 5–9, Jan.–Feb. 1947. 12 refs.

759. Uterus Bicollis Subseptus with Vagina Subsepta. (Uterus bicollis subseptus avec vagina subsepta.)

By A. LENOIR. *Gynaecologia, Basel*, 123, 255–263, Apr. 1947. 5 figs., 6 refs.

Infections of the Reproductive Organs.

760. Absorption of Penicillin from the Vagina.

By M. A. GOLDBERGER, R. I. WALTER, and L. S. LAPID. *Amer. J. Obstet. Gynec.*, 53, 529–531, Mar. 1947. 1 fig., 4 refs.

Penicillin, 500,000 Oxford units, was administered vaginally to 10 patients; 7 were normal menstruating women, 2 had had the menopause, and 1 had had amenorrhoea lasting for 3 months, due to endocrine disorder. Penicillin levels in the blood were determined at intervals up to 3 hours afterwards. The maximum of 1.5 units per ml. on the average was reached in 1 hour, and the level dropped to 0.38 unit at the end of 3 hours. There were wide individual variations. The total urinary excretion in 24 hours varied between 23,425 and 122,000 units. *D. M. Stern*

761. Vaginal Absorption of Penicillin.

By J. ROCK, R. H. BARKER, and W. B. BACON. *Science*, 105, 13, Jan. 3, 1947.

Except during the last 2 months of pregnancy penicillin was well absorbed from vaginal suppositories containing 100,000 units in a base of cocoa butter. Insertion of 200,000 units at one time gave therapeutic blood levels for from 4 to 6 hours. Absorption was poor or undetectable in late pregnancy but good during the puerperium. The suppositories seemed beneficial for vaginal infections and relieved all of 9 patients with vaginitis or chronic cervicitis accompanied by profuse discharge or pruritus or both. *L. Foulds*

762. A Changed Concept of Pelvic Inflammation.

By L. HUNT. *Bull. Vancouver med. Ass.*, 23, 109–112, Feb. 1947.

763. The Treatment of Pelvic Tuberculosis in the Female by Radiation Therapy Based upon Experimental Evidence in the Animal and Clinical Results in the Human.

By R. E. CAMPBELL. *Amer. J. Obstet. Gynec.*, 53, 405–418, Mar. 1947. 4 figs.

This paper considers the radiological aspects of therapy in pelvic tuberculosis as shown by experimental studies in the female dog and clinical investigations in human beings.

Experimentally, dogs of about 12 kg. weight were used. A strain of attenuated bovine tubercle bacilli was selected. It tended to produce localized non-progressive lesions after intrauterine injection at laparotomy. The lesions were inspected at laparotomy at 2-monthly intervals. Photographs illustrate the findings before and after treatment with X-rays at monthly exposures. Of 20 dogs inoculated only 9 were studied over a 2-year period. Seven of the 9 dogs showed arrested tuberculosis, both by macroscopical and microscopical examination. In the remaining 2 dogs there was still evidence of the disease. Only 1 dog died while under treatment. Some of the animals had as many as

8 laparotomies; only in 1 instance did a fistula form. The experiments were controlled.

Seven selected cases of pelvic tuberculosis are discussed. Some patients had sanatorium treatment as well as radiotherapy. A permanent castration effect was aimed at. The author claims to have cured by deep X-ray therapy a fistula of tuberculous origin; he states that " roentgen-ray therapy gave excellent cures in most cases ", and emphasizes that " X-ray therapy is an important adjunct following surgery." Rightly, he condemns this treatment in cases in which there is not positive evidence of tuberculosis.

G. Gordon Lennon

764. Aetiological Study of Adnexal Tuberculosis during the War Years. (Enquête étiologique sur la tuberculose annexielle pendant les anneés de guerre, déductions clinique et thérapeutiques. (A propos de 80 observations récentes.))
By G. GUILLEMIN and J. MOUSSELON. *Lyon. chir.*, 42, 79–88, Jan.–Feb. 1947.

Between 1932 and 1939, only 20 cases of tuberculosis of the adnexa were seen by the authors, while between 1940 and 1945 altogether 80 cases were seen in the same out-patient clinic and in private consulting practice. This fourfold increase is attributed to insufficient food, increased physical work, and, finally, worry due to war conditions. In 3 cases the tubercle bacillus was found in the pus, in 44 cases tuberculosis was proved by laboratory methods, and in the remaining 33 cases the diagnosis was so obvious clinically and at operation that laboratory proof was considered unnecessary and superfluous. Six patients were under 20 years of age, 40 were between 20 and 30 years of age, 28 were between 30 and 40 years of age, and 6 were over 40 years of age (the oldest patient was a 3-para of 59 years of age, who developed tuberculous salpingitis 10 years after her menopause). In 34 cases there was a history of a previous illness which was possibly or certainly of a tuberculous nature: in 15 cases, pleurisy; in 6, peritonitis; in 3, pulmonary tuberculosis; and in 10, various lesions such as cervical adenitis, erythema nodosum, cutaneous tuberculides, and renal tuberculosis. Eight patients had tuberculous relatives. Twenty-six of 50 hospital patients were married, 9 of whom had had children while 3 more had had miscarriages; 18 patients were admitted with acute symptoms of salpingitis and / or peritonitis, while 62 were treated for chronic symptoms (22 had pain in the back or pelvis without pyrexia, 15 had dysmenorrhoea, 16 complained of sterility, 9 had metrorrhagia, 1 complained of amenorrhoea, and 1 had a fistula following appendicectomy.)

The treatment carried out was as conservative as possible. Six of the 18 patients with acute symptoms died. The operative procedures carried out were: in 7 cases, bilateral salpingectomy only (3 deaths); in 3 cases, unilateral salpingectomy and oöphorectomy; in 2 cases, bilateral salpingectomy and oöphorectomy (2 deaths); in 2 cases, total hysterectomy (1 death from tuberculous meningitis); in 2 cases, subtotal hysterectomy and in 2 cases, laparotomy only. There were no deaths among the 62 chronic cases: 35 had bilateral salpingectomy only, 16 had laparotomy only, 4 had unilateral salpingectomy and oöphorectomy, 4 had a repair of a Fallopian tube, 2 had bilateral salpingectomy and oöphorectomy, and 1 had a total hysterectomy. In addition in 20 cases resection of the pre-sacral nerve was carried out at the same time as the main operation. Drainage was never used and all patients made an uneventful recovery. Of the total of 74 patients surviving, only 52 could be followed up: 2 had amenorrhoea, 1 had dysmenorrhoea, and 1 complained of frigidity.

Nicolas Tereshchenko

765. Female Genital Tuberculosis. (Consideraciones sobre tuberculosis genital femenina.)
By N. ARENAS. *An. brasil. Ginec.*, 22, 365–369, Nov. 1946., 2 figs.

766. Female Genital Tuberculosis. (Para a casuistica da tuberculose genital feminina.)
By A. DE MOREAS and C. DO. AMARAL. *An. brasil. Ginec.*, 22, 255–262, Oct. 1946. 3 figs., 37 refs.

767. Genital Tuberculosis with Atresia of the Vagina and Amenorrhea.
By R. T. SCHMIDT and R. L. FAULKNER. *Amer. J. Obstet. Gynec.*, 53, 695–699, Apr. 1947. 15 refs.

768. Tuberculosis of the Cervix uteri. (Tuberculosis del cuello de útero.)
By N. ARENAS, O. BLANCHARD, and J. C. LASCANO GONZALEZ. *Obstet. Ginec. lat.-amer.*, 5, 94–103, Mar.–Apr. 1947. 5 figs., bibliography.

769. Aetiology and Treatment of Pruritus Vulvae. (Prispevek k etiologii a therapii pruritu vulvae.)
By Z. BARTUNKOVA-GABRIELOVA. and J. BARTUNEK. *Cas. lek. ces.*, 86, 422–423, Feb., 1947. 4 figs., 9 refs.

770. Clinical Report of the Frequent Association of Trigonitis with Chronic Cervicitis and Vaginitis : Diagnosis and Treatment.
By W. J. REICH, J. L. WILKEY, and M. J. NECHTOW. *Urol. cutan. Rev.*, 51, 82–84, Feb. 1947. 2 figs., 3 refs.

771. Treatment of Chronic Cervicitis. (Contribución al estudio del tratamiento de las cervicitis crónica.)
By E. CREAGH. *Rev. méd.-quirúrg. Oriente.*, 8, 3–15, Mar. 1947. 30 refs.

772. Chronic Salpingitis.
By H. N. SHAW and J. GASPAR. *West. J. Surg.*, 55, 81–86, Feb. 1947. 3 refs.

The authors have reviewed 3,242 case histories of patients admitted with the diagnosis of chronic salpingitis to the Los Angeles County General Hospital from 1940 to 1945. After eliminating cases of fibroid, malignant tumour of the uterus and ovary, endometriosis, ectopic pregnancy, and pelvic laceration, a study of 759 cases in which surgery was indicated is analyzed in terms of preoperative management and operative procedure. The majority of patients were in the 20 to 40 age group. Some 40 per cent had had abortions. Emphasis is laid on the value of total and differential leucocyte counts and of the erythrocyte sedimentation rate, rapidity of which is not an absolute contra-indication to surgery. Preoperative blood transfusion was given where the haemoglobin was under 40 per cent, and after operation if between 40 and 70 per cent. Only 73 of 730 Wassermann tests gave a positive reaction. Irregular bleeding was a major complaint in slightly over 25 per cent. Eighty-six per cent of patients were discharged in less than 3 weeks.

The difference of opinion on the need for hysterectomy together with bilateral salpingectomy is discussed. Supravaginal hysterectomy was performed in 716 cases and total hysterectomy in 11. The authors believe that deterioration of the ovary after hysterectomy is not due to absence of endometrium but to operative disturbance of the ovarian blood supply. If the venous return is impaired cystic degeneration is inevitable. Adequate preliminary cauterization of the cervical canal is stressed, together with curettage in cases of irregular bleeding. Details of 11 fatal cases in the series are given (gangrene of ileum due to volvulus, 1; subphrenic abscess and tuberculous sigmoid sinus, 1; tuberculous peritonitis, 1; general peritonitis, 4; pneumonia and heart disease, 1; faecal fistula, 2). The eleventh patient died on the forty-first postoperative day [the cause is not definitely stated]. Sulphonamides were not found of use where an old chronic pyosalpinx or a walled-off abscess was present, but should be used in initial attacks, in acute exacerbations, and where infectious material is spilled during operations. The importance of adequate pre-operative care and the use of Wangensteen suction or the Miller-Abbott tube in postoperative distension are stressed. Unless innocuous, the appendix should be removed.

[Exact operative findings as regards pathology and bacteriology are not given.]

C. W. Kimbell

773. **Study of the Ovary in Salpingitis. IV. Operation Conserving Sexual Function in Adnexitis.** (Estudios sobre el ovario anexitico. IV. Comunicacion: La operación conservadora de la funcion sexual en las anexitis.)
By A. SOPENA IBANEZ. *Rev. esp. Obstet. Ginec.*, 5, 225–232, Oct. 1946. 13 refs.

774. **Penicillin Treatment of Gonococcal Infection in the Female.** (La penicilline dans le traitement de la gonococcie féminine.)
By C. BECLERE. *Gynéc. Obstét.*, 45, 813–816, 1947.

775. **Schistosomiasis Mansoni of Genital Tract.** (Comprometimento do aparelho genital na esquistosomose de Manson.)
By M. A. JUNQUEIRA. *Rev. Ginec. Obstet.*, 11, 366–376, Dec. 1946. 5 figs., 11 refs.

New Growths of the Reproductive Organs.

776. **X-ray Treatment of Malignant Tumours in Gynaecology.** (Die Strahlenbehandlung der bösartigen Geschwülste in der Gynäkologie.)
By R. K. KEPP. *Dtsch. med. Wschr.*, 72, 34–38, Jan. 17, 1947. 6 refs.

777. **X-ray Therapy in Non-malignant Gynaecological Conditions.** (A roentgenterapia nas ginecopatias não malignas.)
By A. DE MORAES and J. B. LOBO. *An. brasil. Ginec.*, 22, 237–254, Oct. 1946. 26 refs.

778. **The Diagnosis of Genital Cancer.** (Basle Experience during 1942-1945). (Die Diagnosestellung des Krebses am weiblichen Genitale. Basler Erfahrungen 1942-1945.)
By D. GADOLA. *Gynaecologia, Basel*, 123, 108–125, Feb. 1947. 8 figs., 51 refs.

779. **Vaginal Smear in the Diagnosis of Gynecologic Cancer.**
By W. E. BROWN, O. F. KRAUSHAAR, and J. T. BRADBURY. *J. Iowa St. med. Soc.*, 37, 155–157, Apr. 1947.

780. **Pseudomucinous Cyst (Miller) with Atypical Epithelial Proliferations in a 14-year-old.** (Su di un caso di pseudomucincistoma secondo Miller con note di notevole ed atipica proliferazione epiteliale in quattordicenne.)
By B. MAZZULLO. *Ginecologia, Torino*, 13, 182–193, Apr. 1947. 5 figs., 17 refs.

781. **Fibroxanthoma of the Labium Majus.** (Fibroxantoma do grande lábio.)
By O. DE BARROS SERRA DORIA. *Rev. Ginec. Obstet.*, 1, 259–267, Mar. 1947. 3 figs., 10 refs.

782. **A Case of Hydradenoma of the Vulva.** (Sobre um caso de hidradenoma da vulva.)
By J. RODREGUES LIMA. *An. brasil. Ginec.*, 22, 289–298, Oct. 1946. 9 figs., 13 refs.

783. **Metastatic Chorionepithelioma of the Lung Treated by Lobectomy.**
By H. C. MAIER and H. C. TAYLOR. *Amer. J. Obstet. Gynec.*, 53, 674–677, Apr. 1947. 4 figs.

784. **Endolymphatic Stromal Myosis.**
By D. N. HENDERSON. *Amer. J. Obstet. Gynec.*, 52, 1000–1013, Dec. 1946. 13 figs., 3 refs.
The clinical and pathological characteristics of seven unusual uterine tumours, whose cells re-

semble those of the endometrial stroma, are recorded. The tumours are similar to those previously described as adenomyoma without glands, endolymphatic fibromyosis, and stromal endometriosis. In all the cases the uterus contained one or more tumour masses, the largest being 24 cm. and the smallest 6 cm. in diameter. The tumours were both interstitial and subserous in site, and in 5 cases formed sessile and polypoid growths of varying size which occupied the uterine cavity. They were non-encapsulated and of soft encephaloid consistency. On section they were faintly yellow in colour and homogenous in texture. Radiating from the larger tumours were cords of tumour tissue which infiltrated the myometrium. For the most part these masses appeared to lie in the vascular and lymphatic channels and could be pulled free from the myometrium as slender worm-like strands of rubbery tissue. Extension into the broad ligaments was evident in 5 cases, particularly so in the areas about the uterine vessels, where finger-like cords of tumour protruded from the cut vessels.

Histologically, the cells of the tumours resembled those of endometrial stroma. They were remarkedly uniform in size, shape, and staining qualities. A characteristic and constant feature was the presence of numerous thick-walled blood vessels resembling the spiral arteries of the endometrium, and varying from small capillaries to thick-walled muscular arteries. Where the tumour joined the myometrium the edge was irregular and similar to normal endometrium. The myometrium was not hypertrophied to any great extent, but was deeply invaded by cords of tumour extending between muscle bundles and along perivascular and perilymphatic spaces. These strands of tumour often pushed their way into lymphatic channels. There was invasion of blood vessels, though this was more difficult to demonstrate. In 5 cases direct continuity between the endometrium and the intramural tumour mass was evident. By means of special staining methods a basket-weave reticulum surrounding the individual tumour cells could be demonstrated.

No distinctive symptoms or signs were associated with these tumours. In 1 case menstruation was undisturbed; in the remainder bleeding was irregular and profuse. The age of the patients varied between 28 and 45 years. The physical signs resembled those of uterine fibromyoma and led to an erroneous diagnosis in 6 of the 7 cases. All patients were subjected to bilateral salpingo-oöphorectomy and hysterectomy, and 5 patients later received high voltage X-ray therapy. Only 1 of the 7 patients has died. The longest period since operation is 9 years (2 cases), and the shortest 3 years. The cells of these tumours are slow-growing and well differentiated and do not show the usual malignant characteristics. Nevertheless, the widespread invasion of the lymphatic channels and, to a lesser extent, of the blood vessels is an attribute

of sarcoma. Yet no metastases have been seen in spite of the fact that in 6 cases surgical removal of the tumour was incomplete. These unusual features of the lesion are undoubtedly difficult to explain. It has been suggested that these growths are dependent on oestrogen stimulation from the ovary. The author believes that the tumour may be dependent on its own vascular system for nourishment and growth, and that extensions beyond the uterus are like the branches of a tree rather than its roots. Thus hysterectomy results in severance of the blood supply and death.

Like most of the cases in the literature, the present cases were originally diagnosed as of sarcoma. In the author's opinion the lesion should be regarded as one of low-grade malignancy with a tendency to late local recurrence. He is uncertain of its relation to endometriosis, but the clinical and pathological features of the condition are sufficiently distinctive to warrant its separate classification. "Endolymphatic stromal myosis" is the name he suggests for these neoplasms.

R. L. Hartley

785. Lipomas of the Uterus. (Zur Kenntnis der Fettgewebsgeschwülste des Uterus.)
By P. T. IKONOMOU. *Krebsarzt*, 2, 164–172, Apr. 1947. 57 refs.

786. The Background of Cancer of the Corpus.
By J. A. CORSCADEN and S. B. GUSBERG. *Amer. J. Obstet. Gynec.*, 53, 419–431, Mar. 1947. 8 figs., 35 refs.

The factors relating to cancer of the body of the uterus which are considered in this paper are controlled throughout by comparison with those relating to cancer of the cervix. The average age of women with carcinoma of the corpus was found to be 6.6 years higher than that of women with cervical cancer, a difference less than that usually given; the weight of women with corpus cancer was found to be greater by 18 pounds (8.1 kg.), a significant amount, although some difference is accounted for by the different average age. Of 206 women with carcinoma of the corpus 24.8 per cent were unmarried as against 5.6 per cent of 550 women with cancer of the cervix. Of patients with corpus cancer 38.6 per cent had no children as against 16.6 per cent of the women with cervical cancer. Among women with body carcinoma 37 per cent of marriages were infertile. The economic status of women with carcinoma of the corpus is also exceptional, 47 per cent being private patients as against 23.8 per cent of patients with cancer of the cervix. The age incidence of the menopause showed a peak at 52 to 54 years, and the incidence of excessive and irregular bleeding during the cessation of menses was greater than in the general female population.

Some 1,100 women who had been sterilized by radiotherapy because of bleeding due to benign

causes were studied for an average of 6.7 years. Nine of 15 cases of cancer of the uterus were in the corpus, three times the expected rate. In 31 per cent of cases in which the uterus had been curetted for bleeding during the menopause there was hyperplastic endometrium due to the patient's own endocrine imbalance or to the administration of oestrogenic substances. There was no constant evidence of hyperplasia in the uteri of patients who developed corpus cancer.

It appears, therefore, that cancer of the corpus may develop in unmarried or married and childless women who are overweight and in comfortable circumstances, particularly if the menopause is characterized by excessive bleeding.

[While much has been written about chronic cervicitis as a forerunner of cancer of the cervix, little has been said about the aetiology of cancer of the body of the uterus, and from this point of view this contribution is valuable.]

G. Gordon Lennon

787. The Radiotherapeutic Treatment of Cancer Corporis Uteri.

By J. HEYMAN. *Brit. J. Radiol.*, 20, 85-91, Mar. 1947. 11 figs.

The head of the Gynaecological Department of the Radiumhemmet, Stockholm, following his well-known work on carcinoma of the cervix, has now published an account of his method of treating carcinoma of the corpus uteri by radium. He states that cancer of the corpus is not such a rare disease as is generally believed, forming in his clinic 20 to 25 per cent of the total cases of carcinoma of the uterus seen. He believes that this figure is low, as many cases are referred for hysterectomy to specialists and general surgeons, whereas most cases of cancer of the cervix reach his clinic.

At the Radiumhemmet, out of 670 cases of carcinoma of the corpus observed during the period 1914-39 inclusive, the cases technically operable but clinically inoperable and those clearly inoperable amounted to more than 50 per cent of the total. It, therefore, became important to develop a satisfactory radium technique for the treatment of cases unsuitable for operation. He quotes 5-year cure rates obtained by hysterectomy in cancer of the corpus, but could find only four reports which included at least 100 cases. The relative 5-year cure rates in these reports varied from 48 to 55 per cent, the absolute cure rate not being given. He, therefore, suggests that surgical treatment may be less satisfactory than is generally taught, which is an added stimulus to the development of a satisfactory radium technique.

He has developed a combined operative and radium treatment in which the latter plays the most important part, and since 1930 has used a special packing method, placing radium in the uterus—an advance over previous techniques. The main part of the paper describes this method in some detail

and illustrates the radium containers used. Two treatments are given with an interval of 3 weeks. Surgery is resorted to where radiotherapy fails, as shown by repeated bleeding or increase in the size of the uterus. There is no difficulty in removing the uterus after properly conducted radium treatment; subtotal hysterectomy suffices in most of the recurrent cases. Surgery is sometimes used as the primary form of treatment for cases where cancer is associated with large fibroids, as these cases are difficult to treat with radium because of the irregularity of the cavity. All cases are reported whether treated or not. They are divided into clinically operable, technically operable, and inoperable. A patient is registered as technically operable if the operative risk is great on account of pronounced adiposity, old age, or some associated disease.

The technique of examination and treatment is given in detail. Of 698 cases reported, 670 were treated. The absolute 5-year cure rate was .52 per cent, with a relative cure rate of 54.2 per cent for the whole period. The relative cure rate for the clinically operable was 67 per cent, for the technically operable 48 per cent, and for the inoperable 28.7 per cent. The relative 5-year cure rate for those patients (316) treated by the new method from 1934 to 1939, 22 of whom were operated on after failure of radiotherapy, was 64.9 per cent. This compares very favourably with the results of hysterectomy previously published, where the corresponding cure rate varied from 48 to 55 per cent, in spite of the fact that only operable cases were included in these reports.

D. W. Smithers

788. Cancer of the Uterine Cervix after Subtotal Hysterectomy. (Le carcinome du col restant après hystérectomie subtotale.)

By G. SAEGESSER. *Gynaecologia, Basel*, 123, 89-107, Feb. 1947. 38 refs.

The author notes the great variation in statistics of the incidence of carcinoma of the cervix after subtotal hysterectomy. He has studied cases collected at the University Gynaecological Clinic at Geneva between 1930 and 1945, and discusses the frequency of the condition, the latent interval between the operation and the appearance of carcinoma, the relation between the performance of hysterectomy and the appearance of carcinoma, and prophylaxis.

Out of 620 subtotal hysterectomies performed at Geneva the author collected 12 cases of carcinoma of the cervix (1.9 per cent). Clinical details of these cases are given, and the results compared with those of others who give incidences varying from 0 to 6.09 per cent. Global statistics collected in this way may, however, prove fallacious. The choice between total and subtotal hysterectomy should depend on the state of the cervix at the time of operation. Total hysterectomy is the more

mutilating operation, but must be employed in the presence of cervical lesions. The author states that the incidence of carcinoma of the cervix is less alarming than would appear from recently published figures, and suggests that hormonal disturbances after subtotal hysterectomy may predispose to carcinoma. In view, however, of the extreme frequency of carcinoma of the cervix, its occurrence after subtotal hysterectomy may be regarded as pure coincidence. Evolution in these cases is more rapid than in carcinoma of the cervix with an intact uterus. Treatment is by radiotherapy, but the prognosis is less good than it is in cases where the uterus is intact. The greater operative risk of total hysterectomy is considered more important than the risk of carcinoma, though the need for careful pre-operative examination of the cervix is stressed.

[The battle between the advocates of total and subtotal hysterectomy has gone on for many years and is often rejoined. On the basis of the present article, one can hardly regard an incidence of 1.9 per cent as insignificant, nor can the occurrence of 12 cases of carcinoma of the cervix, which might have been prevented by total hysterectomy, be considered negligible.]

Josephine Barnes

789. Treatment of Carcinoma of the Uterine Cervix. Considerations on the Fiftieth Anniversary of the Wertheim Operation.

By F. BUSCHKE and S. T. CANTRIL. *West. J. Surg.*, 55, 152–161, Mar. 1947. 2 figs., 13 refs.

The good progress achieved in the treatment of cancer of the cervix during the 50 years since Wertheim described his operation now makes it possible to cure a considerable proportion of cases. The proportion would be much increased were optimal treatment available to all women suffering from the disease. The best results are obtained from radiotherapy, and the figures published by Regaud over 10 years ago already show a superiority over surgical treatment. Grouping of cases in stages is necessary for evaluation of results, and the authors follow the classification proposed by the League of Nations Statistical Committee in 1937 (a modification of the old one and not yet in general use). The technique is a modification of the method used by the Fondation Curie, Paris, with the vaginal ovoids developed at the Holt Radium Institute, Manchester. The uterus is usually treated first, and the vagina later; treatment lasts about 2 weeks. X-ray therapy is also given (except in stage I) from an apparatus operating at 800 kV. and 4 fields. If treatment has to be given at 200 kV. two extra fields are added. The cervix is avoided, and fields vary in size from 10 × 8 to 14 × 10 cm. Radium doses are given in terms of milligramme hours and of total dosage to all fields, but Parker's measurement of physical doses is described. He has shown that even for a

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large pelvis a dose of 4,500 r is obtained at the pelvic wall. The radium dosage is delivered in about 2 weeks, X-ray dosage in about 6 weeks. The care of the patient during treatment is important and reactions are carefully observed. Reaction of the rectum is the most common and most serious complication. A slight immediate reaction can hardly be avoided, but in the more advanced cases of the disease a small proportion of severe late rectal lesions must ensue if there is to be a chance of cure. These usually heal with proper management but occasionally fibrous strictures may require colostomy. There may also be bladder reactions, but these hardly ever assume serious proportions. Other complications, such as fracture of the femoral neck, have not occurred in this series.

The 5-year cure rate obtained was 83 per cent. with stage I, 56 per cent in stage II, and 38 per cent in stage III. In 130 cases treated from 1935 to 1940 the relative cure rate was 43 per cent.

Ralston Paterson

790. Examination of the Urinary and Lower Intestinal Tracts before Treatment of Carcinoma of the Cervix Uteri.

By L. A. POMEROY. *Amer. J. Roentgenol.*, 57, 453–454, Apr. 1947. 3 refs.

The findings are reported of intravenous pyelography in 271 patients suffering from carcinoma of the cervix uteri, the X-ray examinations being carried out before the beginning of treatment. As the examinations were made by radiologists at several different hospitals the personal equation made some difference in what was considered abnormal. Cases showing "minimal hydronephrosis" and "minimal hydroureter" were therefore excluded; similarly, cases in which there was slow or diminished excretion of the drug were not reported. Abnormalities were found in 44 cases (16.2 per cent); 3 cases showed double hydronephrosis, 19 single hydronephrosis, 19 functionless kidney, and 3 hydronephrosis on one side and functionless kidney on the other. There did not seem to be any relation between former pregnancies and the abnormal pyelographic findings.

Cystoscopic examinations were carried out on 184 cases, 32 of which showed the bladder wall to be deformed by external pressure of the cervical tumour or by actual invasion, but with a normal mucosa; in 3 cases the mucosa was involved by the tumour. The rectum was examined in many of these patients (137 proctoscopic examinations and 145 examinations by barium enema). In 2 patients a small non-malignant rectal polyp was found; in 10 patients (all with far advanced tumours) there was some deformity of the rectum or lower sigmoid, due either to pressure from the cervical tumour or to involvement of the wall of the intestine by tumour. In none of the 10 was the mucosa involved.

L. G. Blair

791. Infectious Granulomatous Lesions of the Cervix.

By F. GUERRIERO and W. B. MANTOOTH. *J. Amer. med. Ass.*, 133, 832–835, Mar. 22, 1947. 21 refs.

A lesion of the cervix that may look fairly typical on speculum examination and cause symptoms very suggestive of carcinoma may be reported by the pathologist as non-malignant. In this paper it is suggested that some of the lesions are infectious granulomata, and that in fact they are not as rare as has been supposed. The pathologist who undertakes to give a more definite diagnosis than " non-malignant tissue " is confronted with a difficult task. To detect tuberculosis of the cervix, granuloma inguinale, syphilis, or chancroid may require much diligent search for characteristic features, and special staining methods may have to be used.

Biopsy of lesions of the cervix suggestive of carcinoma was performed on 123 patients admitted to Parkland Hospital, Dallas, Texas; 20 per cent were reported to be carcinoma, and 5.7 per cent various granulomatous conditions: 2.5 per cent granuloma inguinale; 1.6 per cent tuberculosis; 0.8 per cent each, syphilis and chancroid.

In Britain the percentage of granulomatous lesions would no doubt be considerably smaller; but it would be well for all gynaecologists to bear in mind that they do occur and to seek the co-operation of the pathologist in the difficult problem of their detection. For, as the authors of this paper point out, the clinical course, therapy, psychological effect on the patient, and prognosis are vastly different from those in cases of carcinoma. *T. C. Clare*

792. Indications for Surgery and Radiotherapy in Early Cervical Neoplasms. (Grades I and II.) A Year's Results. (Indications comparées de la chirurgie et de la radiothérapie dans les néoplasmes du col peu avancés; degrés I et II; résultats d'un an.)

By J. N. MULLER. *Gynéc. Obstét.*, 46, 46–55, 1947.

793. Morphology of Carcinoma of the Cervix Uteri and its Significance in Prognosis and Treatment. (Die Morphologie des Kollumkarzinoms und ihre Bedeutung für die Prognose und Therapie.)

By C. LAUTERWEIN. *Z. Geburtsh. Gynäk.*, 128, 17–106, Mar. 1947. 15 figs., bibliography.

794. The Radium Treatment of Cancer of the Cervix. Historical Review.

By F. W. O'BRIEN. *Amer. J. Roentgenol.*, 57, 281–297, Mar. 1947. 83 refs.

795. Results of the Treatment of Carcinoma of the Cervix at the Women's Clinic, Helsinki, in 1931-1940. (Uber die Ergebnisse bei der Behandlungen von Kollumkarzinomen in der Frauenklinik zu Helsinki in den Jahre 1931–1940.)

By V. TURTOLA. *Acta. obstet. gynec. scand.*, 27, Suppl. 4, 1–50, 1947. 1 fig., 72 refs.

796. Conservative Treatment and Therapeutic Test for Endometriosis by Androgens.

By J. C. HIRST. *Amer. J. Obstet. Gynec.*, 53, 483–487, Mar. 1947. 28 refs.

Although androgens will not cure endometriosis they may afford considerable relief of symptoms, especially in cystic endometriosis. The disadvantages of their use are the lack of regressive effect upon hard, infiltrates or fused masses and the occasional induction of arrhenomimetic symptoms. Androgens are not carcinogenic. In the absence of laparotomy the diagnosis of endometriosis must remain in doubt. The method of administration was to inject 150 to 225 mg. of testosterone propionate in oil intramuscularly over a period of 2 or 3 weeks; this was followed by oral administration of 10 mg. of methyl testosterone daily for variable periods up to 3 or more years. In all, 19 cases were treated and, apparently, there was relief of pain in the majority. *D. M. Stern*

797. Lumbago, Sciatica, and Endocrinology: Heterotopic Endometriosis. (Lombo-sciatalgie et endocrinologie. Contribution à l'étude des endométriomes hétérotopiques.)

By J. DAGNELIE. *Ann. d'Endocrinol.*, 8, 26–31, 1947.

An unusual cause of lumbago and bilateral sciatica is recorded. A woman of 32 gave a long history of pain in the back and along the distribution of the sciatic nerves; the pain had disappeared during a pregnancy and reappeared 6 months afterwards. It was also worse during the follicular phase of the menstrual cycle and had been greatly aggravated by an injection of follicular hormone. A thorough investigation was negative save for the finding of two extremely tender nodules in the pelvis on vaginal examination. Pressure on one of these provoked pain along the back of the left leg. A 9-months course of testosterone (10 mg. four times a month) was given with complete relief from pain after the first injection. When the injections were temporarily stopped the pain returned within 3 months; further injections caused it to disappear again. The pelvic nodules have become smaller and less tender. It is assumed that the cause of the pain was pressure on nerves by nodules of heterotopic endometrium. *S. S. B. Gilder*

798. Endometriosis. (Endometriose. Casuística e etiologia.)

By L. MACHADO and J. F. WERNECK. *An. brasil. Ginec.*, 23, 16–19, Jan. 1947.

799. Endometriosis of the Intestinal Tract.

By M. R. SUTLER. *Univ. Hosp. Bull., Ann. Arbor*, 13, 18–19, Mar. 1947. 2 figs., 23 refs.

800. The Aetiological, Experimental and Clinical Problem of Adenocarcinoma of the Endometrium. (El problema etiologico, experimental y clinico del adenocarcinoma del endometrio.)

By A. Riesco Undurraga. *Rev. méd. Chile.*, **75**, 46–53, Jan. 1947. 21 refs.

801. Uterine Gynatresia and Endometrial Carcinoma. (Ginatresia uterina e câncer endometrial.)

By O. Vaz. *Arch. brasil. Med.*, **36**, 351–360, Sept.–Oct. 1946. 2 figs., 7 refs.

802. Problem of Generalized Abdominal Carcinomata of Ovarian Origin. (El problema de los carcinomas generalizados del vientre de origen ovárico.)

By F. Fonesca and A. Ordonez Acuna. *Rev. méd. Hosp. gen.*, **9**, 505–514, Apr. 1947. 19 figs., 7 refs.

803. Co-existing Different Tumors of the Ovaries.

By S. L. Siegler and L. M. Silverstein. *Amer. J. Obstet. Gynec.*, **53**, 700–703, Apr. 1947. 3 figs., 10 refs.

804. Perforating Ovarian Cystic Teratomas: Report of an Unusual Case.

By G. H. Lowe. *Proc. Mayo Clin.*, **22**, 117–120, Mar. 19, 1947. 2 figs., 15 refs.

805. Teratoblastoma of the Ovary. Teratoblastoma do ovário.)

By A. Peltier de Queiroz. *Rev. Ginec. Obstet.*, **1**, 202–212, Feb. 1947. 9 figs., 4 refs.

806. Endocrine Ovarian Tumours. Virilizing Lipid Tumours. (Tumores ováricos endocrinos. Tumores lípidos masculinizantes.)

By A. M. de la Riva. *Rev. esp. Obstet. Ginec.*, **6**, 94–107, Mar.–Apr. 1947. 17 figs., Bibliography.

807. A Case of Arrhenoblastoma of the Left Ovary. (Un caso clínico de tumor virilizante del ovario izquierdo tipo arrhenoma.)

By J. C. Graham and C. Villasenor. *Rev. méd. Hosp. gen.*, **9**, 372–383, Feb. 1947. 13 figs., 13 refs.

808. Virilizing Ovarian Tumors.

By J. Pedersen. *J. clin. Endocrinol.*, **7**, 115–129, Feb. 1947. 6 figs., 30 refs.

809. Ovarian Fibroma and Myoma (Meigs's Syndrome). (Fibroma e mioma ovarianos—sindrome de Meigs.)

By O. Vaz. *Arch. brasil. Med.*, **36**, 1–12, Jan.–Feb., 1947. 4 figs., 14 refs.

810. Contribution to Ovarian Dysgerminoma. (Beitrag zum Disgerminoma ovarii.)

By V. Grunberger. *Klin. med.*, Wien, **2**, 202–211, Mar. 1, 1947. 2 figs.

811. Dysgerminoma of the Ovary. (Disgerminoma do ovário.)

By W. Maltez. *An. brasil. Ginec.*, **22**, 384–392, Nov., 1946. 6 figs., 19 refs.

812. Spontaneous Amputation of Fallopian Tube Following Torsion of a Cyst. (Amputácia tuby spôsobena torziou cysty.)

By E. Dlhos. *Bratislavské lekárs. List.*, **27**, 80–87, Feb. 1947. 2 figs., 5 refs.

813. Primary Cyst of the Round Ligament.

By M. A. Castallo and B. J. Giletto. *Amer. J. Surg.*, **73**, 320–325, Mar. 1947. 10 figs., 52 refs.

The purpose of this paper is to review the available literature on cysts of the round ligament and present a further case of true primary cyst of that structure. The authors distinguish this type of cyst from hygromas and cystic degenerations of solid tumours by the fact that it is unilocular and lined by a single layer of columnar or cuboidal epithelial cells. Of the 52 cases of cyst of the round ligament collected from the literature only 12 were found to conform to these criteria. The authors add another case of their own in which the outer third of the round ligament was involved. The cyst was unilocular and microscopical examination showed that its thin fibrous connective-tissue wall was lined by a single-layer of flattened, cuboidal, epithelial cells. The embryological development of the round ligament in relation to the rest of the female generative organs is well described and illustrated by several figures. The conclusion drawn by the authors from the embryological survey is that the origin of a true cyst of the round ligament is in a developmental anomaly of the Wolffian body.

R. L. Hartley

814. Haemoangio-endothelioma of the Broad Ligament. (Emoangioendotelioma del legamento largo.)

By P. Quinto. *Riv. ital. Ginec.*, **29**, 329–356, 1946. 10 figs., bibliography.

815. On the Origin of Certain Perisalpingeal Cysts.

By R. A. Reis. *Amer. J. Obstet. Gynec.*, **52**, 964–974, Dec. 1946. 12 figs., 8 refs.

Isolated nests of cells are often encountered in the walls of the Fallopian tubes. These nests, in the author's view, consist of transitional cells, and morphologically resemble very closely those described by Limbeck and Brunn in the urinary tract (*Z. Heilk.*, 1887, **8**, 55, and *Arch. mikr. Anat.*, 1893, **41**, 294). The cells in the centre of these nests often become liquefied and form cysts, whereupon the cells lining the degenerated areas assume cuboidal shape. The origin of rare adenocarcinomata arising in the urinary bladder has been traced to these cuboidal cells. The author advances the hypothesis that these cell nests and cysts seen so often in the tubes may arise from misplaced urinary tract epithelium, and may provide the site of origin for certain carcinomatous growths involving the Fallopian tubes.

Two cases of carcinoma of the tubes are discussed. The first was a case of primary papillary transitional-cell carcinoma. In the second case there was a tumour involving both tube and ovary, its cells presenting features of transitional epithelium together with glandular structures. The suggestion is made that both growths originated in cell nests.

[There is nothing to be found in this paper which contradicts the impression that the cell nests described are Walthard islets. It is now generally accepted that these cell nests are the origin of Brenner tumours. They are found more often in the wall of the Fallopian tube than in the ovary.]

R. L. Hartley

816. Primary Carcinoma of the Fallopian Tube. [In English]

By E. BLOCK. *Acta. radiol., Stockh.,* 28, 49–68, Feb. 28, 1947. 31 refs.

Primary cancer of the Fallopian tube is rare. During the years 1922-45, 16 such cases were admitted to the Radiumhemmet, Stockholm. The literature is reviewed, and the author points out that only 12 of the 479 cases reported since 1847 have shown 5-year cures. In each Radiumhemmet case the diagnosis was analysed. Six were definite cases of primary tubal cancer, but incomplete surgical records preclude certainty about the other cases. The histological picture does not indicate the organ of origin, and the differential diagnosis between carcinoma of the ovary and of the tube is, therefore, impossible in advanced cases.

Of the 16 cases, 4 were bilateral, 9 left-sided, and 3 right-sided. The ages of the patients were: 28 years (1 case), 41 to 45 years (2 cases), 46 to 50 years (5 cases), 51 to 55 years (3 cases), 56 to 60 years (4 cases), and 61 to 65 years (1 case). Eight patients were in the menopause, while 4 were in the transition period. Ten had had children, and 1 an ectopic gestation and an abortion. In 1 case only was there a previous history of salpingitis, but microscopical examination showed inflammation in the non-cancerous portion of the tube in 5 of the 12 cases. In 2 cases tuberculosis was found with the cancer. In 9 cases the carcinoma was situated in a hydro- or pyo-salpinx. The tubes were evenly thickened in 2 cases, while the others showed tumours varying in size from a hen's egg to a child's head. At operation the growth was seen to be confined to the tube in 7 patients, the rest showing involvement of ovary, peritoneum, or uterus. No metastases were seen before or at operation, but in 1 case, at necropsy 3½ months after operation, widespread metastases were found. Cancer at two different sites was seen in 2 cases. Other coincidental findings were ovarian cysts and fibroids. Of the 16 tumours, 11 were adenocarcinomata and 5 papillary growths. The symptoms were discharge, bleeding, pain, and, in 1 case, increasing size of the abdomen alone. The correct diagnosis was not made before operation in any case, and in 4 only by the pathologist. The essential factor in prognosis is the spread of the growth. All patients whose growths were confined to the tubes are alive and free from evidence of disease, while the others died within 3 months to 4 years after operation.

It is a routine at the Radiumhemmet not to remove the uterus when salpingo-oöphorectomy is performed for carcinoma of ovaries and tubes. Radium placed in the uterus comes in closer contact with the area of recurrences than that placed in the vagina. The radiological treatment is by intrauterine or vaginal radium application followed by X-ray treatment to two anterior and two posterior fields. The radium dose varies, in the uterus between 990 and 1,500 mg. hours, in the vagina between 1,800 and 3,000 mg. hours. The X-ray dose varies also. In later years a dose of 3×400 r has been given to each of 4 fields in the first series, followed 3 months later by a second series of 2×400 r to each field. After another 6 months a dose of 1×400 r is given.

Of this series 7 patients are living and free from evidence of disease after 22, 10, 10, 4, 3, and 2 years, and 1 year respectively. Of the rest, at the time of operation 4 growths had involved pelvic peritoneum and the operation was necessarily incomplete. In 5 cases, recurrences were present at the time the patient was admitted to the Radiumhemmet. One patient was in such poor general condition that the treatment could not be completed. Nevertheless, of these, 2 were kept relatively free from signs and symptoms for 4 and 3 years respectively.

Lilian Raftery

Operations.

817. Hormone Treatment in Operations for Carcinoma of the Female Genitalia. (Hormonbehandlung bei Karzinomoperationen am weiblichen Genitale.)

By E. PREISSECKER., *Krebsartz,* 2, 57–60, Feb. 1047.

Corpus luteum hormone lowers the tonus of the bladder muscle while follicular hormone raises it. The use of follicular hormone to improve the weakened tonus of the bladder, particularly marked after hysterectomy for carcinoma, seems to the author a logical procedure. During a radical hysterectomy a considerable amount of bladder denervation must take place, so that bladder function is always disturbed post-operatively, and complete emptying on micturition does not occur for 3 to 4 weeks. This has two disadvantages: (1) catheterization is required, and (2) post-operative X-ray irradiation must be delayed until bladder function is restored.

To 11 patients who had undergone a Wertheim operation the author has given injections of 2.5 to 5-mg. of follicular hormone daily, up to a total of 50 mg., beginning on the day after operation; he considers that this has shortened the period of bladder dysfunction by 6 to 10 days. A further advantage of the hormone treatment is that dilatation of pelvic blood vessels leads to improvement in blood supply to the operation area, so that healing is more rapid. The author now advises implantation under the peritoneum covering the parametrial stump of a 50 to 100 mg. pellet of oestradiol or

an equivalent product, supplementing this for 28 days with intramuscular injections of follicular hormone. This is particularly recommended where the patient has not already reached the menopause, in order to relieve the symptoms due to her artificial menopause. *S. S. B. Gilder*

818. Essential Factors in Preoperative, Operative, and Postoperative Care of Gynecological Patients.

By C. M. JOHNSON. *New Orleans med. surg. J.*, 99, 320–327, Jan. 1947. 8 refs.

819. Sulphonamido-penicillin Therapy in the Treatment of Laparotomy Complications. (La sulfamido-penicilinoterapia en el tratamiento de las complicationes laparotomicas.)

By B. BRAVO LOPEZ. *Toko. ginec. práct.*, 6, 35–40, Jan.–Feb. 1947.

820. Chemical Sacral Sympathectomy in Gynaecology. (La simpáticectomia química sacra en ginecologia.)

By J. GOMEZ-SIGLER. *Toko-ginec. práct.*, 5, 405–413, Dec. 1946. 2 figs., 35 refs.

821. The Making of an Artificial Vagina with the Aid of the Membranes from a Foetus at Term. (Création d'un vagin artificiel a l'aide des membranes ovulaires d'un oeuf à terme.)

By A. BRINDEAU, P. LANTUEJOUL, and L. HUBERT. *Gynéc. Obstét.*, 45, 418–422, 1946, 7 figs., 1 ref.

A well-built woman, aged 21, with normal secondary sex characters had never menstruated but had vague symptoms of malaise each month. Examination disclosed absence of the vagina, and no trace of a uterus could be found. Laparotomy showed the presence of two ovaries of normal size full of small corpora lutea, all of the same dimensions. To each ovary was attached a tube terminating in a tiny reniform uterus. The two uteri were joined by a transverse fold of peritoneum. At the patient's request it was decided to construct a vagina from the membranes of a full-term foetus, a procedure which the authors had used twice previously. Accordingly, while the next Caesarean section was being performed in the clinic, the patient was placed in the lithotomy position under general anaesthesia and a U-shaped incision was made as for a perineorrhaphy. A tunnel 6 cm. long was dissected up between the bladder and rectum almost up to the pouch of Douglas, and into this was placed a large piece of the membranes, both amnion and chorion, from the Caesarean delivery. The piece of membrane was pushed into the tunnel on the end of a Hegar dilator, its apex fixed to the fundus of the tunnel with a catgut stitch, and its edge sutured to the edges of the skin incision. The vagina thus fashioned was packed with ribbon-gauze soaked in horse-serum, the packing being withdrawn at the end of a week and renewed daily until epithelialization was complete. After discharge the patient was asked to introduce a size 20 Hegar dilator daily into the vagina. The chorio-amniotic graft gave a very satisfactory result. *S. S. B. Gilder*

822. An Evaluation of Certain Factors Pertinent to Surgery of the Anterior Vaginal Wall.

By I. F. FROST. *Urol. cutan. Rev.*, 15, 67–71, Feb. 1947. 4 figs., 5 refs.

823. On the Risk of Infection in Connexion with Examinations for Sterility, with Special Reference to Hysterosalpingography. (Om Infektionsrisiko ved Sterilitetsundersogelser med særligt Henblik paa Hysterosalpingografi.)

By O. L. OLESEN. *Ugeskr. Læg.*, 109, 41–45, Jan. 9, 1947. 31 refs.

The author reports 7 cases of pelvic infection with one death, following hysterosalpingography (HSG). There was no history nor were there signs of inflammation before the HSG in the fatal case (though subsequent curettings showed endometritis and postmortem showed a pelvic peritonitis spreading from the genitalia). In another case evidence of inflammation was rather vague and the infection that followed was not acute. In the other 5 cases, there was evidence in the history or on examination of some previous infection and serious, acute inflammation followed, usually bilaterally, in about 3 weeks. Three of the 7 patients had a curettage 48 hours after the HSG and 2 others had had an insufflation of the tubes the day before.

In none of the cases was there evidence of acute infection, but the author considers that even in its absence HSG carries a risk. Errors of technique doubtless play a part, but the risk appears to be increased if there is evidence of even mild chronic infection, especially if the Fallopian tubes are shown not to be patent. Some workers (Proust *et al.*, *Bull. Soc. Gyn. Obst.*, 1936, 25, 348 and Douay, *ibid.*, p. 514) suggest immediate salpingectomy to prevent infection in the latter patients, as they are in any case sterile, and they should certainly be watched carefully for some weeks. The author does not now perform a curettage while the patient is in hospital for the HSG. Many of the earlier papers dealing with the evidence of infection after HSG (or foreign-body reaction in uninfected cases) are quoted in brief, and the author stresses the need for careful follow-up. *A. M. M. Wilson*

824. Ligature of the Internal Iliac Arteries in Hysterectomy. (La ligadura de las arterias hipogástricas en las pan-histerectomias abdominales ampliadas.)

By M. S. BRAGA. *Rev. Asoc. méd. argent.*, 60, 1015–1018, Nov. 30, 1946. 13 refs.

The author summarizes his results with ligature of the internal iliac arteries in 5 cases of hysterectomy for carcinoma of the cervix. No postoperative complications supervened and all patients were alive when this article was written some 2 years after the operation. In all the cases

the ligation was performed immediately distal to the origin of the superior gluteal artery.

J. Trueta

825. Technique of Intra-isthmic Total Hysterectomy. (Technique de l'hystérectomie totale intra-isthmique.)

By C. Elbaz. *Presse méd.*, **17**, 194, Mar. 19, 1947. 3 figs., 3 refs.

The relative advantages and disadvantages of total and subtotal hysterectomy are well recognized. One of the disadvantages of the former is the disturbance of the supports of the vaginal vault with the danger of encouraging subsequent prolapse. The technique here described is one which can be applied to non-malignant conditions of the uterus. It consists in removing the epithelium of the cervical canal by coring out the cervix between the longitudinal and circular fibres. This leaves the ligamentary supports unaffected. It is important that the clamps applied to control the uterine vessels should be applied at a lower level than when a subtotal operation is performed. If this is done there is no danger of haemorrhage. The author states that over 400 such hysterectomies have been done at Hertz's Clinic without any untoward incident, and in no case has prolapse followed.

Kenneth Bowes

826. Hysterectomy in a Small General Hospital.
By W. C. Scrivner and J. D. Belleville. *Illinois med. J.*, **91**, 199–201, Apr. 1947.

827. Vaginal Hysterectomy in Non-malignant Conditions of the Uterus. (Histerectomia vaginal nos processos não malignos do útero. Indicações e detalhes de técnica.)

By O. da Silva Loureiro. *An. brasil. Ginec.*, **22**, 276–281, Oct. 1946.

828. A Report on Experience with Vaginal Hysterectomy.
By H. C. Stearns. *West. J. Surg.*, **55**, 220–235, Apr. 1947. 19 figs.

829. Modification of Schauta-Wertheim's Operation. (Modificación de la operación de Schauta-Wertheim.)

By J. L. Jimenez Martin. *Rev. esp. Obstet. Ginec.*, **6**, 108–113, Mar.–Apr. 1947. 7 figs.

830. Conservative Surgery of the Ovaries. (Cirugia conservadora de los ovarios.)

By C. Zuckermann. *Rev. Mex. Cir. Ginec. Cáncer*, **15**, 107–112, Mar. 1947.

831. Limitations of Colposcopy. (Limites da colposcopia.)

By J. P. Rieper. *An. brasil. Ginec.*, **22**, 282–288, Oct. 1946. 4 figs.

832. Multiple Myomectomy. (Les myomectomies multiples.)

By C. Roman. *Gynéc. Obstét.*, **48**, 62–67, 1947.

833. Conservative Surgery of Uterine Fibroids and Sterility. (Konservativní operace délozního myomu a sterilita.)

By J. Nesnidal. *Ceskoslov. Gynaek.*, **12** (26), 95–98, 1947.

834. When to Operate in Cases of Uterine Retroflexion. (Quandos operar os retrodesvios uterinos.)

By A. A. Quinet. *Med. Cirurg. Farm., Nos.* 130-131, 102–107, Feb.–Mar. 1947.

835. New Orthopaedic Treatment of Uncomplicated Uterine Retroflexion. (Neue orthopädische Behandlung der unkomplizierten Gebàrmutterknickung.)

By F. Lichtenstein. *Zbl. Gynäk.*, **69**, 222–225, 1947. 1 fig.

836. Posterior Colpotomy for Diagnosis of Pelvic Diseases.

By A. Decker. *Amer. J. Surg.*, **73**, 313–319, Mar. 1947. 12 refs.

The author has previously published a number of papers describing the technique and value of posterior colpotomy as a diagnostic procedure in cases of obscure pelvic disease. The method of inserting a trocar and cannula into the posterior pouch to allow an endoscope to be introduced into the pelvis for visualization of the pelvic viscera was first described by the author and a colleague. This procedure of endoscopic visualization by cul-de-sac puncture the author now terms "culdoscopy". Later he extended the method so that the phenomenon of spontaneous pneumoperitoneum could be utilized as an aid in the radiological diagnosis of pelvic disease and in testing tubal patency.

The purpose of the present paper is to emphasize the reliability of the knee-chest position in preference to the more frequently adopted lithotomy position. The scope and details of the technique of "culdoscopy" are also enlarged, the author having acquired more experience. The principal reason why puncture of the pouch has not achieved popularity as a diagnostic aid in cases other than those of atypical ectopic pregnancy is that with the patient in the lithotomy position there is either failure of entry or lack of a confirmatory sign to suggest that the pouch has been successfully punctured. To overcome these difficulties the author commends the knee-chest position. The vagina thus distends; the posterior vaginal wall becomes thin, and the distance between the cervix and the rectum is increased. Furthermore, the negative intra-abdominal pressure so created will enable proof of entry to be established. In fact, provision must be made to prevent the entrance of air, otherwise a spontaneous pneumoperitoneum of from 600 to 1,800 ml. will occur—a phenomenon utilized for radiological diagnosis.

Little preparation is necessary when the procedure is used to remove fluid or introduce air. The patient assumes the knee-chest position. The perineum is elevated with a Sims speculum, and

the vagina painted with antiseptic solution. The cervix is grasped with a volsellum and drawn down; a 4½-in. (11.4-cm.) No 22 gauge needle attached to a 20-ml. syringe with the plunger drawn half-way out is pushed into the posterior pouch. When the peritoneal cavity is entered air will be aspirated from the syringe. If it is desired to produce an air pneumoperitoneum, the syringe is removed. Carbon dioxide can be substituted by attaching a length of rubber tubing from a bag containing the gas to the needle. When the purpose of the puncture is to determine the presence of fluid or blood, a small trocar and cannula fitted with a valve is substituted for the needle. When the instrument is correctly placed the patient is turned to a supine position to allow the pelvic contents to escape or be aspirated. The technique for endoscopic visualization of the pelvic viscera differs in some details. The procedure is carried out with full operating-room facilities. The patient is given either 100 mg. pethidine or 3 gr. (0.2 g.) sod. " amytal " 45 minutes before examination. The table must be equipped with upright leg holders and shoulder braces to maintain the knee-chest position. Before insertion of the trocar and cannula the site of the puncture is anaesthetized with a few ml. of 2 per cent procaine. It is recommended that carbon dioxide be substituted for air in endoscopy as it has the advantage of rapid absorption.

Puncture of the pouch has now been carried out by the author in more than 400 cases, mostly for endoscopic diagnosis. Various pathological entities of the pelvic organs have been observed. Particular mention is made of the possible value of the method for determining ovulation by direct inspection of the ovary. Recently some minor therapeutic measure, such as aspiration of cysts and release of thin adhesions, have been attempted. The author has not observed any complications resulting from puncture of the pouch when carried out in the knee-chest position. There has been a varying amount of distress where an air pneumoperitoneum has been induced. The procedure is contra-indicated in the presence of acute vaginal infections or where a fixed mass fills the pouch and does not move when the knee-chest position is assumed; moreover, it is impossible when cardiac or debilitated conditions do not permit assumption of the posture for even a few minutes.

R. L. Hartley

837. Bilateral Simultaneous Uretero-intestinal Implantation by Davalos's Method in the Treatment of Incurable Vesico-vaginal Fistula. (Uretero-êntero-anastomose bilateral simultânea pela técnica de Davalos, no tratamento das fistulas vésico-vaginais incuráveis.)
By A. DE AQUINO SALLES and A. A. COURI. *An. brasil. Ginec.*, 22, 263–275, Oct. 1946. 3 figs.
The technique described by Davalos was em-

ployed with success in 3 cases of vesicovaginal fistula of long standing in which other treatment had failed. The operation steps are described. The main advantages are: (1) a transverse incision in the sigmoid in the line of the vessels interferes much less with the blood supply; (2) with the incisions in the serous and muscle coats on the one hand and submucous and mucous coats on the other at different levels a valve-like arrangement is obtained so that the increase of pressure in the sigmoid shuts the mouths of the ureters; (3) the two ureters are dealt with at the same operation. In 2 cases the only complication was anuria (for 1 day), treated by intravenous administration of saline. The second patient developed peritonitis in the second week but recovered after drainage of the peritoneal cavity. The anuria is explained by oedema of the ureteric orifices and periureteritis. The peritonitis was probably caused by leakage. All the patients had 2 days' preparation with sulphasuxidine and intestinal lavage with dilute hydrogen peroxide. The first case reported was operated on just over a year before the paper was written.

Jorge D. Mineiro

838. Ureterocystoneostomy in Uretero-vaginal Fistulæ (2 Cases). [A ureterocistoneostomia nas fistulas ureterovaginais. (A propósito de dois casos).]
By O. VAZ and C. RODRIGUES. *Rev. méd. munic.*, 9, 120–132, Oct.–Dec., 1946. 23 refs.

839. Successful Repair of a Vesicovaginal Fistula Complicating Carcinoma of the Cervix.
By W. C. SCRIVNER. *Amer. J. Obstet. Gynec.*, 53, 694, Apr. 1947.

Urology.

840. Urological Gynecology.
By D. LAZARUS. *Urol. cutan. Rev.*, 51, 74–75, Feb. 1947.

841. Urology in Gynecology.
By J. M. BROCKMAN. *Urol. cutan. Rev.*, 51, 76–78, Feb. 1947.

842. Differential Diagnosis between Gynecological and Urogenital Diseases.
By B. LIEGNER. *Urol. cutan. Rev.*, 51, 84–86, Feb. 1947. 2 figs., 2 refs.

843. Pelvic Abscess and its Relation to Urological Conditions.
By R. W. HUSSONG. *Urol. cutan. Rev.*, 51, 78–80, Feb. 1947.

844. Treatment of Incontinence of Urine by Suspension of the Urethra with a Fascia Lata Sling. (Tratamiento de la incontinencia de orina por suspensión de la uretra con una cincha de fascia lata.)
By E. A. FOX and M. BESSONE. *Rev. méd.-quirurg. Patol. fem.*, 14, 419–427, Oct. 1946. 5 figs., 5 refs.

Vaginal operations fail to cure many cases of stress incontinence, and the operations of the Göebel-Stoeckel and Alridge type, though more successful, are difficult and produce some weakening of the abdominal wall. The authors have, therefore, devised a method of using fascia lata which they consider to be easy and to have little risk if carried out according to their technique. They describe this method in detail and include 3 cases.

A strip of fascia lata, 14 cm. long by 1 cm. wide, is first removed and placed aside in gauze. The patient is then put in the gynaecological position in such a way that both the suprapubic and vaginal fields of operation are exposed. A transverse incision 6 cm. long, 3 cm. above the upper border of the pubis, is then made in the skin of the abdominal wall and deepened to the aponeurosis, which is exposed in the whole length of the incision. The wound is packed with gauze and the vaginal part of the operation started. With the vaginal wall held on the stretch with forceps an incision is made in the midline from a point 2 cm. behind the urethral meatus to the region of the bladder neck, the mucous membrane only being divided. A number 5 or 6 Hegar dilator is passed into the urethra in order to determine its position, the degree of its displacement, and the position of the bladder neck. The dilator is also used to place the vaginal septum on the stretch, and this is then incised 1½ cm. outside the urethra and parallel to it, the incision being 3 cm. long. Into the opening thus formed, the index finger is introduced, and by blunt dissection a tunnel is formed in the prevesical space. In order to avoid injury to the bladder or important vessels the finger is kept close to the pubic bone. The dissection is carried as far as the posterior surface of the rectus muscle immediately above the pubis. The same procedure is then carried out on the other side. With a finger in one of these tunnels the surgeon guides upwards a ligature-carrier till its tip reaches the posterior surface of the rectus muscle. An assistant then determines the position of the tip by palpation, and the muscle and aponeurosis are perforated immediately above the pubis and 2 cm. from the midline. A strong ligature attached to the strip of fascia lata is then threaded through the eye of the instrument, and by means of this the end of the strip is pulled downwards and then passed upwards on the opposite side through the other tunnel, the muscle being perforated in a similar place. The assistant then pulls on the ends of the strip of fascia, while the surgeon, with the dilator still in position, verifies that the fascia is placed at the junction of the urethra and bladder neck and that the canal is suspended against the pubis without undue obstruction. When a suitable degree of tension has been achieved, the ends of the strip are fixed by sutures, the excess is removed, and the incision closed. Catheterization is necessary for some days. The authors consider that the operation could be simplified by using ribbon gut, as advocated by Lowley, or ox fascia, which Chandy found to be of value in experimental work.

A full clinical report is given of 3 cases in which this operation was carried out. The first patient was 53 and suffered from almost complete incontinence. Over 2 years after operation the patient remained free from urinary symptoms. The other 2 cases were less severe but the results were satisfactory. In one of them a preliminary abdominal myomectomy was carried out. In both there was slight suppuration of the abdominal wounds.

[Fascia lata has previously been used in these operations, but Studdiford has found that it sloughs out. In the cases reported here it appears to have been used very successfully, and the most severe case has been followed up over an adequate period.]

Bryan Williams

845. **Traumatic Gynatresia with Formation of Urinary Calculus in the Vagina.** (Ginatresia de origen traumatico con formación de cálculo urinario en vagina.)

By S. Dexeus and M. Dalmau. *Rev. esp. Obstet. Ginec.,* 5, 333–337, Dec. 1946. 6 figs.

846. **Pollakiuria at the Terezin Camp.** (Theresienstadt.) [De la pollakiurie au camp de Terezin (Theresienstadt).]

By F. Bass and J. Braun. *Gynaecologia, Basel,* 123, 126–130, Feb. 1947.

847. **Reconstruction of the Female Ureters.** (Reconstrução da uretra feminina.)

By A. Monteiro. *An. brasil. Ginec.,* 23, 20–35, Jan. 1947. 2 figs., 27 refs.

Miscellaneous.

848. **Interesting Cases of Torsion of the Uterus.** (Zajímave prípady deloznich torsi.)

By J. Birgus. *Lēk. Listy,* 2, 189–195, Feb. 15, 1947. 4 figs., 10 refs.

849. **Total Genital Prolapse and Rectal Prolapse.** (Prolapso genital total e prolapso retal por invaginação procidente.)

By G. De Oliveira. *Rev. Ginec. Obstet.,* 1, 272–292, Mar. 1947. 9 figs., 26 refs.

850. **Haemorrhagic Infarction of the Mesosalpinx due to Thrombopoietic Endotheliosis with Vegetations.** (Infarcissement hémorragique du méso-salpinx par endothéliose végétante trombopoiétique.)

By J. Courtois, —. Lelievre, and P. Isidor. *Rev. franç. Gynéc.,* 42, 59–63, Feb. 1947.

851. **Gynaecological Haemoperitoneum.** (Hemoperitoneos Ginecologicos.)

By C. Zuckermann. *Rev. mex. Cir. Ginec. Cáncer,* 15, 59–65, Feb. 1947.

The Fourth of November, 1847 :
James Young Simpson and Chloroform Anaesthesia

BY

JAMES MILLER, M.D.

THE story of the discovery of the anaesthetic properties of chloroform, surely one of the most romantic in the history of medicine, has often been told, but in view of the centenary of the occurrence it is right and proper that it be once more recounted. Ether had been found in 1846 and had been used for the induction of anaesthesia in midwifery and surgery. One man at least—James Young Simpson—was not satisfied, and he bent his great energy and outstanding talents towards the discovery of "something better."

A few days before the 4th November, 1847, Simpson and his private assistant, James Matthews Duncan, a young Aberdeen graduate of 21, went to the laboratory of Dr. Gregory, professor of chemistry, in search of "substances which had respirable vapours." The search was conducted in a lumber room below the seats of the chemistry classroom, and a selected few substances, chloroform among them, were removed to a cupboard in the waiting-room of 52 Queen Street, Edinburgh, the residence of Professor Simpson.

On the day of the discovery Matthews Duncan experimented on himself with these substances and picked out several as deserving of more careful investigation. We have no details of this trial, which was the first time chloroform was inhaled so far as is known, and Matthews Duncan was always very reticent on the subject. He tells us, however, in a letter to Sir Robert Christison, written in 1875, that he took particular notice of chloroform "as the best and likely to be most useful judging from its effects on myself."

The same evening, the 4th November, three men seated themselves at Professor Simpson's dining-room table. In front of each was a tumbler in which about a teaspoonful of the substance to be respired was placed. The tumbler in its turn was immersed in a basin of hot water. "Holding the mouth and nostrils over the vessel's orifice, inhalation was proceeded with, slowly and deliberately; all inhaling at the same time, and each noting the effects as they advanced." Having inhaled several substances, including acetone and benzine, without effect, the trio, Simpson, Duncan and Keith, tried chloroform. "Immediately," as the narrator, James Miller, professor of surgery, says, "an unwonted

hilarity seized the party; they became bright-eyed, very happy and very loquacious—expatiating on the delicious aroma of the new fluid. The conversation was of unusual intelligence, and quite charmed the listeners—some ladies of the family and a naval officer, brother-in-law of Dr. Simpson. But suddenly there was a talk of sounds being heard like those of a cotton-mill, louder and louder; a moment more, then all was quiet and then—a crash. On awaking, Dr. Simpson's first perception was mental—'This is far stronger and better than ether,' said he to himself. His second was to note that he was prostrate on the floor, and that among the friends about him there was both confusion and alarm. Hearing a noise, he turned round and saw Dr. Duncan beneath a chair; his jaw dropped; his eyes staring, his head bent half under him; quite unconscious, and snoring in a most determined and alarming manner. More noise still, and much motion—and then his eyes overtook Dr. Keith's feet and legs making valorous efforts to overturn the supper-table or, more probably, to annihilate everything that was on it. I say, more probably; for frequent repititions of inhalation have confirmed, in the case of my esteemed friend, a character for maniacal and unrestrainable destructiveness—always, under chloroform, in the transition stage."

The experience was repeated many times that night—one of the ladies even taking her turn—until the supply of chloroform was exhausted. This account of the proceedings by Professor Miller is stated by Matthews Duncan and Keith* to be approximately correct.

No time was lost in putting the new anaesthetic to use. The first child born of a mother who received chloroform was

delivered on November 9th. On the 10th Simpson went to the Royal Infirmary where his colleague in surgery had two operations to perform. The first patient was a Highland boy, 4 or 5 years old, affected with necrosis of the radius. Simpson thus describes the effects: " On holding a handkerchief, on which some chloroform had been sprinkled, to his face, he became frightened, and wrestled to be away. He was held gently however and obliged to inhale. After a few inspirations, he ceased to cry or move, and fell into a sound snoring sleep." The operation was then performed, and " Half an hour afterwards, he was found in bed, like a child newly awakened from a refreshing sleep, with clear, merry eye, and placid expression." It is interesting to note that the second surgical case anaesthetised immediately after this one, a soldier with a face operation, showed his approval of the new agent by cramming the sponge soaked in chloroform into his mouth and re-starting the process of administration on his own.

So much for the events of November 1847. Now a few words about Simpson and his associates in the research.

James Young Simpson has been so often the subject of biography that it would be superfluous for me to enter into detail in this short note. My special qualification for the office of recorder is that I am linked to the greatest era of the Edinburgh medical school—the '40s and '50s of last century—by my father who was a pupil of Simpson and by my grandfather, who was one of his colleagues and closest friends. For some years they lived next door to one another, and thus it came about that James Miller was able to relate so intimately the events above described.

Anyone asked to select the half dozen greatest men of Scottish birth in the 19th century would, I feel sure, include Simpson among them. He came of humble origin

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* Keith states that the inhalation was not carried out by all three at the same time.

and rapidly attained to eminence. We are apt to think that the idea of " too old at 40 " is a modern one, but we must remember that of the group of men holding medical chairs in Edinburgh university during the middle of last century almost all received their appointments in their 20's or 30's. Robert Christison was 25 when he became professor, James Syme was 34, James Miller 30 and Simpson 28. His election to the chair of midwifery was secured by a majority of only one vote.

In stature Simpson was short, but he had broad shoulders and his figure, especially in the fur coat which he was accustomed to wear, was squat. He had neither the build nor the skill of a great surgeon. His head was large, and this appearance of great size was enhanced by the thick mane of auburn hair which he wore long, as was then customary. In most of his portraits his expression was genial, but in repose and in some of the pictures which we have the look is sad. That does not mean that he was devoid of wit and humour. Far from it. His house was always full of guests and the host was the centre and soul of the entertainment. Even amateur theatricals were occasionally indulged in, and Eve Blantyre Simpson recalls seeing her father's sturdy form appear before the footlights with a colleague, Lyon Playfair, both dressed in short petticoats as the Babes in the Wood and both sucking oranges and crying lustily.

Simpson's versatility was remarkable. He wrote copiously on many subjects, notably, like Rudolf Virchow, on archaeology. He had no relaxations in the ordinary sense of the word and he played no games. He relished a walk, or a scamper as he called it, and he paid frequent visits to the continent of Europe. He escaped from the insistent calls of his profession by driving down to Trinity, where he had a house three miles from Queen Street and where he enjoyed, as he was accustomed to put it, " a sunset and boiled egg."

His practice was enormous and he drove through the streets of Edinburgh at something approaching a hand gallop, the police having special instructions concerning him. He never wasted a moment. He could be seen standing outside a patient's door while the bell was being answered, with a book in his hand. " How do you get time," asked a patient, " to read all the novels of the day ? " " By never wasting an orra moment," was the reply. He had, like many another man who has reached eminence, the capacity to sleep at any moment and in all circumstances, even in his carriage. But although he usually drove in his carriage to see his patients he was not above climbing long stairs in the Old Town to visit the poor. His patients were devoted to him, and as one old lady said, " His blithe, silvery-toned voice; the lightsomeness he brought in with him, did her more good than any medicines ever invented." Nor was it only spiritual comfort which he scattered. He would remark to some unfortunate that it would be a favour to call upon him for a loan if necessary—" For I was poor too," he said, " and if my brothers hadn't helped me without stint, I would not be where I am to-day."

In money matters Simpson was casual, and his faithful butler was accustomed to collect the guineas from his pockets at the close of a day of consultations. On the other hand he would refuse a fee if he arrived too late to do anything or if the patient's condition was beyond hope. On one occasion he refused a fee of a thousand pounds to attend a lady in Brighton, as he knew her to be a *malade imaginaire*. Very naturally he regarded such a visit as a sheer waste of time.

He was in many ways in advance of his time, as witness his advocacy of the pavilion type of building for hospitals. He proposed

the erection of cheap, one-storied blocks separated from each other by wide air spaces, his idea being to prevent the transference of infection, to allow of the building being taken down readily should an epidemic occur, and behind it all was the notion of the healing power of Nature if left to herself.

He died at the comparatively early age of 59. Like Sir Walter Scott he suffered in his later years from arteriosclerosis. Byrom Bramwell gives an account of what was found at the autopsy. The main cause of death was atheroma of the arteries and an aneurysm the size of a pigeon's egg in the heart. Furthermore, all the organs showed pronounced fatty degeneration, a feature which may not have been unconnected with the repeated use of toxic drugs during his experiments on himself. Even after his discovery of chloroform he continued to test other compounds and was found by his butler on one occasion lying unconscious on his study floor.

His death was widely mourned and a resting place in Westminster Abbey was offered by the nation. His wife, however, chose that his remains should lie in the place in which he had laboured. The headstone in Warriston Cemetery looks up towards the towering dark city, crowned by the Castle rock.

No mention of the discovery of chloroform would be complete without a reference to at least one of Simpson's associates—James Matthews Duncan. As already stated, and as James Haig Ferguson mentions in his presidential address to the Edinburgh Obstetrical Society, "It is an open secret that some of his friends thought he never received the recognition which was due to him for his share in the discovery, as there seems little doubt but that he had previously tested the properties of chloroform upon himself before calling Professor Simpson's special attention to it." Duncan was a man of outstanding ability—manly, blunt, witty and genial. Haig Ferguson describes him as the embodiment of the Hippocratic ideal, the type of the perfect physician. As is well known, after failing to obtain the chair of Obstetrics in Edinburgh following the death of Simpson, he migrated to St. Bartholomew's hospital, London, where he acquired a great reputation for skill as a gynaecologist. He died in 1890 at the age of 64.

Finally, let me remind you that the research which led up to the discovery of chloroform was carried out at the end of a long day of operating, consulting and teaching. Simpson's stock-in-trade was courage, vision and perseverance. His apparatus was of the simplest—a tumbler—and his laboratory was his own dining-room.

Diagnostic and Therapeutic Aspects of Kymographic Uterotubal Insufflation with Comparative Observations on Hysterosalpingography*

BY

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ANY discussion of the diagnostic procedures employed nowadays in the investigation of sterility in the female calls to mind the striking departure from the casual examination which was practised by gynaecologists as well as by family physicians at the beginning of this century. The superficial examination could scarcely be expected to throw much light in the cause of the sterility. It consisted for the most part of making a bimanual examination, upon the findings of which were formulated prognosis and therapeutic advice.

Inspection of the vagina and cervix by means of the speculum and the occasional exploration with the uterine sound ventured by the more thoughtful gynaecologists and general practitioners shed little more light on the situation. Based upon the meagre findings obtained by the use of these simple physical aids, procedures were devised that constituted the the alpha and the omega of the measures calculated to cure sterility.

These mistakes were inevitable because the upper portion of the genital tract, namely the Fallopian tubes, were inacessible to ready exploration. An exploratory laparotomy for the sole purpose of determining the anatomical condition of the Fallopian tubes was deemed a formidable procedure. For laparotomy was not without serious hazards in those days and it was therefore both feared by patients and hesitantly performed by gynaecologists.

This impasse was finally surmounted by hysterosalpingography and soon thereafter by uterotubal insufflation. Both procedures arose as a result of the realization, some 3 or 4 decades ago, that many of the surgical operations formerly employed to relieve sterility were futile and ill-considered. In 1914 Cary and Rubin independently published the idea of injecting X-ray-opaque substances into the uterus for the specific purpose of determining, without recourse to laparotomy, whether the Fallopian tubes are open or closed. Cary reported using collargol and published his paper in the *American Journal of Obstetrics*, March 1914. Rubin also used collargol and published his paper in the *Zentralblatt fur Gynäkologie*, May 1914. The work upon which Rubin's report was based was done at the II Universitat Frauenklinik of which Von Rosthorn was the head. The paper was submitted for publication in February of 1914.

As both these papers were published just before the first world war we did not become aware of similar work by others until some years later. Douay presented some historic data in his report before the 5th Congress of the Association of French Gynaecologists and Obstetricians at Lyons,

September 1927. In this report Douay stated that Lelorier was the first to inject an isotonic non-irritant fluid into the uterus with the object of determining tubal patency. His results were to have been presented before the Congress at Lille in 1912, and were never published. Lelorier believed that if 20 ml. of this fluid were injected and none returned from the cervix, it was proof that the Fallopian tubes were patent.

According to Douay's report, Dimier deserves credit for being among the first to inject into the uterus a fluid opaque to the X-rays. Dimier's attempts were made in 1913 upon patients in the Broca Hospital, under the direction of Pozzi. He used a 10 per cent solution of collargol and injected 7 to 8 ml. Inasmuch as one patient died of peritonitis, Pozzi made Dimier abandon his research. Owing to the first world war the paper was not published until 1916, when it appeared over the signature of Dartigues.

According to Schultze, however, the first recorded attempt to use a radiopaque substance was made by Rindfleisch who used an emulsion of bismuth in 1910. The Roentgenographic shadows obtained by this method were poor and apparently did not encourage others to employ it.

I record these facts because they illustrate the parallel and almost simultaneous response to an apparently long-felt need for a method that would enable us to diagnostic patency or non-patency of the Fallopian tubes without resorting to exploratory laporatomy.

Use of these substances all had the same objective, namely to visualize Roentgenoscopically the lumen of the Fallopian tubes. They were followed in rapid succession by sodium bromide, sodium iodide, and thorium nitrate, 1914 to 1919 (Rubin). Kennedy's report on the use of sodium bromide in 1923 apparently gave impetus to wider application of hysterosalpingography. Sodium bromide had been previously abandoned by Rubin and gained no permanent adherents. It was soon supplanted by iodized oils, which found their chief form in lipiodol. Introduced by Siccard and Forrestier in 1922 lipiodol was first employed in gynaecology by Carl Heuser in 1923. Other contrast-media soon thereafter came into use but not as extensively as lipiodol. These substances were lipo-iodine, thorotrast, umbrathor, iodochloral and the soluble crystalloid iodine substances. Skiodan with acacia (Titus) and viscorayopaque (Rubin) are the most recent developments. In these media it was sought to combine the physical properties of viscosity with relatively rapid resorbability.

I have used practically all these radiopaque substances but not without realizing the disadvantages attaching to the majority of them. Having begun my work with the attempt to demonstrate the presence of submucous myomata which were notoriously refractory to X-ray treatment and to radium as used about 1914, I have come to realize that hysterography *per se* has a place in the study of sterility which is invaluable. There is need, however, to emphasize once more, as I have been at pain to emphasize on previous occasions, that salpingography has drawbacks that are not sufficiently appreciated. It is not generally realized that once the Fallopian tubes are filled with lipiodol they frequently cannot, if the tubes are stenosed or obstructed, rid themselves of the oil, especially if it is trapped at some point of the ampullary portion.

Hysterosalpingography has been compared, by some of its advocates, to barium X-ray of the intestines. There is one difference which makes that comparison invalid, because the oil cannot be cleared out of the Fallopian tube as barium can be

evacuated from the colon. If barium is retained in the colon and is not spontaneously expelled, it can be eliminated by enema or purgatives. Retention of lipiodol is due to the fact that peristalsis is partially or totally inhibited by the pathologically altered muscle of the tubal walls. This prevents the tube from ridding itself of the retained iodized oil, which is too viscous to pass through a stenosed point in the tubal lumen. When there is no tubal obstruction the oil can find its way into the peritoneal cavity whence it disappears after varying lengths of time.

My 'early experience with collargol, which was found to remain inspissated in the lumen of normal Fallopian tubes, led me away from the use of radiopaque substances which included the halogen salts that I sought to substitute for collargol. Later work with lipiodol resulted in similar findings. Foreign-body granulomata produced by retained lipiodol were not infrequently encountered. The foreign-body reaction is induced by persistence of the iodized oil at tight points in the lumen which are nevertheless permeable to some slight degree, as previously determined by insufflation with carbon dioxide. In such cases the ultimate result is that permanent occlusion replaces permeable' strictures.

I feel that gas could not possibly induce such changes and hence began to use oxygen for injection into the uterus in November 1919.

Oxygen was found to be satisfactory as a gaseous medium, but it caused pains in the shoulders which persisted for from one to several days. This disadvantage was soon relieved by substituting carbon dioxide, which is rapidly resorbed and, if the patient is placed in the Trendelenburg position at once, the shoulder pains disappear promptly and do not return when she rises from the examining table. Thus a perfectly harmless gas is tolerated while it serves to establish the fact of tubal patency or non-patency, and has the advantage over radiopaque substances that it leaves no residue. The gas rises promptly from the pelvis to the subphrenic space where it is rapidly resorbed. Its applicability to manometric control, in contrast to what is physically more difficult to obtain in oil injection, and the combination of a kymograph have made uterotubal insufflation a safe and scientific clinical method for testing for tubal patency and various degrees of tubal obstruction.

The point of the physical difference between gas and fluid has not been sufficiently appreciated by many workers, one might almost say most workers who employ lipiodol or other iodized oils exclusively. The ideal radiopaque substance which shall fulfil all the requirements for clinical diagnostic purposes, including rapid disappearance from the Fallopian tubes under all circumstances, has not yet been achieved. Its nearest approach has been realized in viscorayopaque, which is a combination of a crystalloid iodine substance—diethanolamine salt of $2:4$ dioxo-3- iodo-6- methyltetrahydropyridine acetic acid—with polyvinyl alcohol. The latter gives it a viscosity which has been intentionally made to equal or exceed the viscosity of lipiodol. Viscorayopaque nevertheless is followed, despite all attempts to the contrary, in a certain number of cases by pelvic pain not unlike the reaction attending and ensuing after lipiodol injection. This disability, which it produces alike with the iodized oils and the halogen salts, is not as long in duration and can be obviated by analgesics such as demerol, or a combination of codein, phenacetin and aspirin which may be given prophylactically.

In contrast to this reaction following the intrauterine injection of radiopaque solutions there is no pelvic pain whatever

after the insufflation of carbon dioxide. Since the gas rises to the subphrenic space as soon as the patient sits up or stands, the pain is localized in the shoulders and, as has been said before can be made to disappear promptly by the reclining posture. But carbon dioxide gas leaves no residue within the Fallopian tubes and hence does not induce permanent occlusion in stenotic but partially patent Fallopian tubes. It has a further advantage that it can be used repeatedly for therapeutic purposes, an advantage not shared by radiopaque solutions.

An advantage claimed by many who employ hysterosalpingography exclusively is that by this method the site of occlusion or partial stenosis may be graphically demonstrated. I have been able by careful control with roentgenography of the tubes to show that the site of obstruction can be equally diagnosed by means of kymographic uterotubal insufflation. It only requires careful notice of the radiation of the momentary pain which accompanies the insufflation, the same or less intense pain that is encountered during hysterosalpingography. Many observations at laparotomy, preceding and following uterotubal insufflation, and experimental studies have corroborated the interpretation of the pain-radiation. In combination with the salpingograph obtained by kymographic uterotubal insufflation, the diagnosis of the site of obstruction can be made in practically all cases, or, to put it another way, for all practical purposes.

It should be noted in this connexion that the interpretation of the lipiodol films is subject to considerable difference of opinion in many cases, and that it requires much experience and skill to establish the fact of patency or not in an appreciable number of instances. When in doubt, it is much safer and more convenient to repeat uterotubal insufflation than to inject lipiodol. I shall not enter further into other details which have been published in my monograph and elsewhere concerning this point. But one item of considerable importance must be mentioned, namely, that the hazards of lipiodol-injection are greater than those attending or following uterotubal insufflation and that, after repeated injection of iodized oils in the same patient, these hazards are vastly greater than after repeated insufflation.

I have, for example, insufflated one patient, with secondary amenorrhoea of 10 years' duration, more than 50 times for scientific purposes over a period of several years without the slightest untoward sequelae. Sharman has done daily insufflations on several patients throughout several menstrual cycles without encountering any reactions. This cannot be said of repeated injections of lipiodol which it would be foolhardy to use to the same degree. Schultze reported a pelvic infection following a second salpingography. One may obtain a fair comparison between the incidence of infections after injection of lipiodol from Gauss's report on 3,000 collected cases, which he found suitable for critical review, and the report obtained in answer to my personal questionnaire in 1928, which included 6,821 insufflations from various sources. There were 13 infections following the 3,000 injections of lipiodol, an incidence of 1 in 230 cases; there were 4 infections following the 6,821 insufflations, an incidence of 1 in 1,705 cases.

Schultze analyzed 8,000 lipiodol cases from the literature and found 27 complications, about 1 in 300 cases. In a later and larger personal questionnaire comprising 80,376 tubal insufflations, the incidence was 0.0024 per cent (1 in 423) representing 190 pelvic infections. This incidence naturally includes various factors such as lack of experience on the part of many employing

insufflation, in the same way as inexperience undoubtedly is accountable when lipiodol is used. If the indications and contra-indications are constantly borne in mind, and the method is carried out correctly, there need be no accidents when uterotubal insufflation is employed. An illustration of this statement is the report of George Gray Ward and Albert H. Aldridge who had not encountered a serious accident in 3,000 insufflations.

There was a total of 15 embolisms reported in all answers to the questionnaire comprising the 80,376 insufflations. Twelve cases recovered and 3 died. It is noteworthy that in one well-documented group comprising 17,177 insufflations there were 3 embolisms and all 3 recovered. In another less-documented group comprising 41,472 insufflations there were 6 embolisms and 1 died. In a small group comprising 7 per cent of all the replies there were recorded 5 embolisms, 3 of which resulted in death. The reporters of this group did not give permission for publication of their names. Embolism occurred only when air or oxygen was used. There were no deaths following insufflation with carbon dioxide. The physical properties of carbon dioxide, chiefly its solubility in equal volumes of fluid and its rapid resorbability, account for its absolute safety.

Although I do not use iodized oils or even viscorayopaque for tubal diagnosis except in rare cases, I believe there is still excellent use for hysterography *per se* in sterility and for other gynaecological conditions. One can get a good idea of the inner configuration of the uterus and demonstrate the presence of polypi and submucous myomata, of adenomyosis and developmental anomalies such as bicornuate uterus and the like, by means of uterine radiography, and I have employed this method as far back as 1914 for this purpose. It will probably hold its place as a diagnostic procedure in sterility as an alternative to uteroscopy, which will undoubtedly be more frequently employed in the future.

Diagnostic Aspects of Uterotubal Insufflation.

The technical procedure employed in the last 22 years includes use of a kymograph in combination with a manometer and tank of carbon dioxide, and may therefore be termed kymographic, uterotubal insufflation. By means of this apparatus all the essential diagnostic data may be obtained with reference to patency, non-patency, partial stenosis, tubal spasm and hypotonicity. These 5 categories comprise all the physiological and pathological conditions of the Fallopian tubes as encountered in clinical practice and they will be discussed briefly in the order named.

Normal tubal patency is characterized by a relatively low initial rise of pressure usually below 100 mm. Hg, followed by a more or less sharp drop, which is soon succeeded by manometric oscillations ranging between 10 and 30 mm. Hg in amplitude (Fig. 1) indicating that the tubes are undergoing rhythmic contractions. By auscultation one can hear an intermittent tubal souffle in the lower abdomen in each hypogastric fossa or sometimes only in one. This does not mean that the other tube is necessarily closed; it may be due to the fact that the "silent" tube has a narrower uterine ostium or that it is hypertonic. When the patient sits up after the insufflation, for a brief minute or two she experiences pains in one or both shoulders. These pains can be promptly relieved by placing the patient in the Trendelenburg position for a few minutes; she is then able to go about her ordinary duties.

Tubal non-patency. Instead of dropping to or below 100 mm. Hg, the pressure rises to 200 mm. Hg, without exhibiting any oscillations and, when the gas flow is
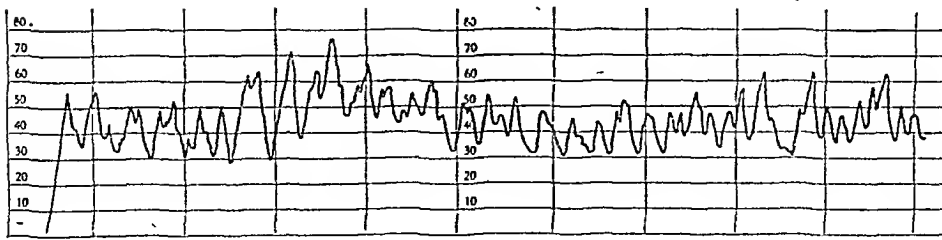
FIG. 1.

Rhythmic contractions in normal tubal patency with normal menstrual cycle. Note continuation of rhythmic contractions for 10 minutes. The patient was insufflated for 40 minutes in order to produce a large pneumoperitoneum. The contractions persisted throughout the insufflation.

stopped, a horizontal line is described on the kymograph (Fig. 2, facing p. 744). There are no pains in the shoulder because a subphrenic pneumoperitoneum has not been produced.

The carbon-dioxide is trapped within the Fallopian tubes at some point distal to the uterine openings or at the uterotubal junction (Fig. 2). The patient experiences temporary local pain during the insufflation, the character of which varies with the site of obstruction and whether the latter is symmetrical or asymmetrical. Careful notice of the pain-reaction affords diagnostic data as to the location of the site of obstruction. In general, when pain is suprapubic the obstruction is at the uterine ends of the tubes. When the pain radiates outwards the point of obstruction is located beyond the uterine ends, the wider radiation indicating greater proximity to the fimbria.

These points have been checked by X-ray-opaque media in hysterosalpingography (Fig. 2), by observations at laparotomy, and by experimental duplications of pathological conditions.

Partial stenosis. Obstructed Fallopian tubes which permit carbon dioxide to pass through them at points below 200 mm. Hg yield on uterotubal insufflation curves that differ from normally patent tubes and totally occluded tubes. The pressure in such cases rises to a point well above 100 mm. Hg and, instead of dropping sharply, declines in a gradual paraboloid fashion without exhibiting typical oscillations. These depend upon the degree of the stenosis and its cause, whether muscular inflammatory infiltration, or peritubal adhesions and kinking of the lumen. A subphrenic pneumoperitoneum is produced, resulting as a rule in symptoms referred to the shoulder. But in some cases the gas is trapped in the pelvis and fails to rise to the subphrenic space because of pelvic adhesions. When the tube lumen is not constricted but the tube is bound down for all or most of its length, the initial pressure is not necessarily high but there are at most, feeble, if any, manometric oscillations, i.e., tubal contractions are diminished in frequency and amplitude (Fig. 3).

It should be noted that if the abdomen is auscultated the souffle will be heard as a constant purring instead of being intermittent as is the case in normal patency.

Uterotubal spasm is characterized by a relatively high initial rise of pressure above 100 mm. Hg followed by a sharp drop, which is succeeded by rhythmic oscillations as in normal patency (Fig. 4). The spasm may be overcome at the first trial or the pressure may have to be maintained for a few seconds before the uterotubal sphincter relaxes, following which the gas
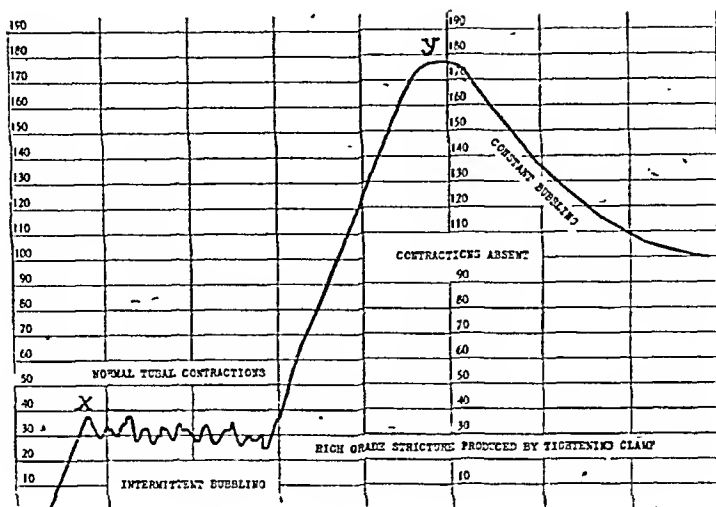
FIG. 3.

Showing the effect of constriction (stenosis) upon tubal
contractility. Note pressure increase from 38 mm. Hg at
X, to 178 mm. Hg at Y, after constriction and resultant
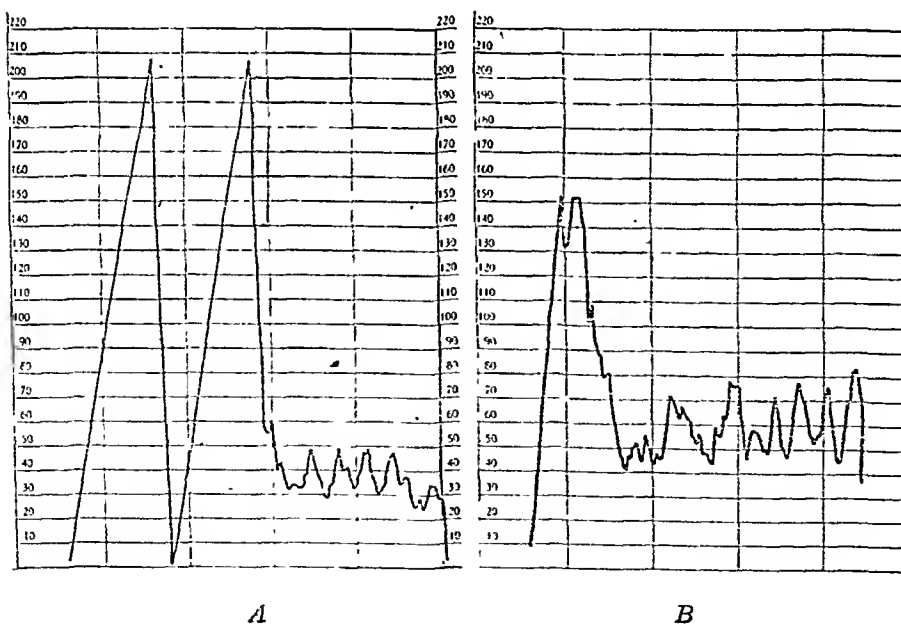abolition of contractions.

FIG. 4.

A, B. Two examples of uterotubal spasm.

passes through the tubes in a normal fashion. A subphrenic pneumoperitoneum and shoulder pains result in normal patency. The spasm may be overcome at once or the pressure may have to be maintained for a few seconds before the uterotubal sphincter relaxes, following which the gas passes through the tubes in a normal fashion. A subphrenic pneumoperitoneum and shoulder pains result as in normal patency.

A *fifth condition is encountered* in patent tubes whose musculature is atonic. The kymographic tracing is characteristic of prolonged primary and secondary amenorrhoea (Fig. 5). · After artificial castration by X-rays and the natural menopause this atonic condition is most frequently met.

Peritubal adhesions and tubal stenosis. A clinical analysis of the findings with respect to the occurrence of peritubal adhesions and tubal stenosis showed the following: There were 538 cases of tubal adhesions or 16.75 per cent of the general group and 379 cases with permeable strictured tubes (11.84 per cent).

Uterotubal spasm. There were 97 cases out of 2,014 of the primary sterility group or 4.81 per cent; and 37, or 3.12 per cent of the 1,186 secondary sterility group. Antispasmodics of all descriptions have been used. The ideal pharmaceutical antispasmodic is not yet available. Luminal, transantin phenobarbital-syntropan, papaverine have seemed to be useful when administered for several days before insuf-
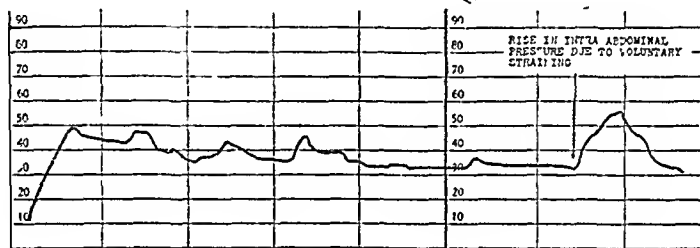
FIG. 5.

An example of low-tone, shallow contractions of Fallopian tubes in a case of prolonged secondary amenorrhoea. Note the rise in pressure due to voluntary straining.

The incidence of these conditions, as encountered in a personal series of 3,200 cases which were analyzed in 1937, are as follows: 814 or 40.41 per cent. of 2,014 cases of primary sterility had normal patency, and 396, or 33.39 per cent of 1,186 cases of secondary sterility could be classified within normal limits of patency.

Non-patency was encountered in the total series in 29.34 per cent, 536 cases of non-patency, or 26.61 per cent of the 2,014 primary sterility patients, and 403, or 33.98 per cent of the 1,186 secondary sterility cases.

flation. Amyl nitrite used immediately before the test has seemed to relax the spasm. · Pelvic-abdominal diathermy immediately preceding the insufflation has also been found useful in some cases. By and large, insufflations alone done properly, without trauma or use of a cold cannula, the pressure being maintained for a minute or two in the obdurate cases, succeeds in overcoming · spasm. As has been seen it is met in 1 out of 20 or 25 cases.

The therapeutic possibilities of uterotubal insufflation were suggested by Ruben Peterson, who was one of the first of the

important gynaecologists to adopt this procedure. He was largely responsible for its popularity throughout the United States and I record this fact with sincere appreciation and reverence for his memory. Peterson employed transuterine pneumoperitoneum not only to diagnose tubal patency and non-patency but also for treatment of obstructed tubes, for the relief of dysmenorrhoea and to establish pneumoperitoneum for general diagnosis. Rongy was another of the early pioneers who advocated uterotubal insufflations for therapeutic purposes.

Although the question of how insufflation aids the sterile woman has engaged the interest of many workers since Peterson and Cron's first publication, an exact explanation cannot always be given. For the majority of successes the therapeutic action appears to be the following:

(1) It establishes patency of the genital tract from the external os of the cervix to the fimbriated ends of the Fallopian tubes. The cannula acts as a mechanical dilator in narrow cervical canals, and insufflation sometimes dislodges a mucus plug and by clearing the canal permits a fortuitous ascent of spermatozoa.

(2) The same effects may be postulated for the Fallopian tubes in which inspissated mucus may be dislodged from a narrow to a wider area, agglutinated folds become separated and perifimbrial adhesions broken through. The last is probably the most likely.

(3) A possible psychosomatic effect cannot be ignored as sometimes, without encountering tubal obstruction, the mere performance of insufflation may serve as an intense emotional stimulus which relaxes the tubal and cervical sphincters on the one hand, while on the other possibly provoking ovulation in a manner analogous to that which takes place in some of the lower animals. There can be no question of a therapeutic result when the test, which

is repeated once or several times with an improvement in tubal patency is followed shortly afterwards by pregnancy. The therapeutic results of uterotubal insufflation in cases where tubal obstruction was first encountered may be seen from the following table.

TABLE I.

	Number of cases	Number improved	Percentage
Tubal obstruction: maximum pressure 200 mm. Hg	939	185	19.70
Adherent and strictured tubes: maximum pressure 200 mm. Hg or less	917	238	25.95
Uterotubal spasm: maximum pressure up to 190 mm. Hg	134	15	11.19

Altogether, there were 438 patients whose Fallopian tubes showed improvement in patency on a second or third insufflation. Sixty-six (15.07 per cent) of these women became pregnant. It is noteworthy that 70 of the 238 patients with adherent and narrowed tubes showed a normal curve following insufflations. As Peterson has shown by experimental observations during laparotomy, closed tubes in the truest sense may be opened by employing sufficiently high pressures. In many of the other relatively closed or non-patent tubes it is possible to widen the strictured canal by more sustained pressures. From the therapeutic point of view this is of the greatest importance, as experience has repeatedly demonstrated.

From what has just been said it may be stated that within certain clinical and pathological limits practically all Fallopian tubes fall into 3 groups: (1) normally patent tubes, (2) non-patent tubes, (3) intermediary. With adequate pressures, group 2 may be advanced to groups 3 and

1, and group 3 may be more readily restored to group 1, i.e., normality. The extent to which some degree of patency can be produced by tubal insufflation will determine the conceptional possibilities in women whose sterility is traceable chiefly and exclusively to tubal pathology.

A brief analysis of 590 pregnancies which were preceded by uterotubal insufflation may serve to bring out pertinent facts. These pregnancies were reported voluntarily and I have no accurate information as to what eventuated in all of the 3,200 cases out of which number the 590 pregnancies were reported, as no systematic follow-up was carried out. The patients volunteered the information or transmitted it through another patient whom they were kind enough to recommend for similar treatment. For these reasons the percentages adduced cannot be accepted as definite. Furthermore it must be stated in this connexion that there is great difficulty in ascribing proper credit to any method calculated to relieve sterility unless all the circumstances connected with the case are fully available. I am also aware of the tendency to ascribe to any new method of treatment an occasional successful result in the sense of *post hoc ergo propter hoc*. In this group there are patients who became pregnant where the test had only the diagnostic value of determining tubal patency.

The cases have been analyzed from the view-point of the findings with uterotubal

insufflation. Cases of primary as well as of secondary sterility have been included.

Comparison with the natural expectancy of conception. Coghlan has given statistical figures based on a large section of the population of Australia in which he analyzed the natural expectancy of pregnacy after marriage. This has served as the basis for comparison. After the 3rd year 3 times as many patients became pregnant as might be expected from the natural incidence. After 7 years the patients' chances are increased many fold by insufflation; and after 10 years, compared to Coghlan's estimates, insufflation appears to improve proportionately the chances of pregnancy. The 2 patients who became pregnant after having been sterile for 15 years show an incidence of 1 in 1,600 as against 1 in 20,000, according to Coghlan's figures. When it is considered that 34 of my patients were between the ages of 35 and 40 years, and 6 were over 40 years, the 40 pregnancies in this group may be accepted as due to therapeutic efforts rather than chance.

The tubal factor. Insufflation was the only treatment employed in 386 of the 590 patients who became pregnant (65.42 per cent). The therapeutic measures employed in the remaining 204 cases are too varied for evaluation.*

Table III shows that 46.44 per cent of the pregnancies occurred in women whose Fallopian tubes exhibited various degrees of impaired patency.

The incidence of pregnancy in the general sterility group according to the status of the tubes is shown in Table IV.*

The therapeutic effect of insufflation is particularly noteworthy in the 118 cases

TABLE II.
Duration of Sterility (Primary and Secondary).

Years	Number	Percentage
1 to 3	285	48.31
3 to 5	162	27.46
5 to 10	127	21.53
10 to 15	14	2.37
15 to 20	2	0.33
Total	590	100.00

* Nine hundred and thirty-nine of the 3,200 cases of sterility proved to have non-patent tubes and therefore are excluded from the statistics bearing on pregnancy.

TABLE III.

Tubal Status in 590 Patients who Became Pregnant

	Number	Percentage
Normal patency	316	53.56
Adherent tubes	135	22.88
Strictured tubes	118	20.00
Spasm and normal patency	21	3.56
Total	590	100.00

TABLE IV.

	No. of cases	No. of pregnant cases	Percentage
Normal patency	1210	316	26.12
Adherent tubes	538	135	25.09
Strictured tubes	379	118	31.13
Spasm and normal patency	134	21	15.74
Total	2261*	590	21.6

* See note on previous page.

of strictured tubes, for pregnancy was achieved in 31 per cent as against 26 per cent of the cases with normal tubal patency.

Use of the kymograph. The value of the kymograph in these cases cannot be over-estimated. It has been used by me in conjunction with tubal insufflation since May 1925 and, particularly in connexion with prognosis and therapy, it affords appreciable aid. Of the 590 patients who became gravid, 544 were examined with the kymograph. Thanks to increased experience gained through the use of this instrument, is has been possible to repeat the test both with greater intelligence and more gratifying results. Forty-nine patients had been insufflated elsewhere.

Time of pregnancy in relation to insufflation. The time elapsing between insufflation and conception was noted. Data were available in 573 cases.

It is noteworthy that 158 women became pregnant within 1 month after insufflation,

and 70 more within 2 months, making a total of 228 patients (38.64 per cent) who became pregnant within 2 months after insufflation. This short interval appears to be a fair criterion of the therapeutic value of the method. Many of these patients had been married or sterile 5 years and longer. Obviously the test cannot be held to have produced a remedial result when more than 2 regular menstrual periods have intervened between its use and conception except in cases where strictures were encountered. In cases where insufflation has demonstrated normal tubal patency, one can speak only of its diagnostic and prognostic value. The fact that 38 women became gravid in my series after an interval of 2 years or more following insufflation, should cause us to hesitate to give a hopeless prognosis for childbearing when

TABLE V.

Time of Pregnancy in Relation to Insufflation.

Number of pregnancies	Number of months after insufflation
158	1
70	2
37	3
38	4
35	5
40	6

378, or 64.07 per cent, of the pregnancies occurred within 6 months of the test; 108 pregnancies occurred within the second 6 months.

Number of pregnancies	Number of years after insufflation
49	2
15	3
9	4
5	5
3	6
3	7
2	8
1	10

In 17 cases the time interval was not recorded

the Fallopian tubes have been found patent or where they have been rendered patent.

Proof of therapeutic efficacy. If one judges results according to the rigid lines of the criteria for a therapeutic result we have 26 cases which have fulfilled all the requirements. These 26 cases were women who became pregnant within 1 month following this procedure. They were over 30 years of age, had been sterile for a period of over 5 years, had taken no contraceptive precautions for at least 1 year, and had resorted to no other treatment than insufflation. Excluding most of the other cases, there remain 66 in whom a therapeutic action on the part of insufflation is suggested because pregnancy followed upon improvement in the tubal status as a result of repeated insufflations.

In estimating therapeutic results or aetiological factors, the possibility of chance or accident, which must always be taken into account, was seriously considered. In smaller series than the present, chance may have undoubtedly played a large part as it most probably has in a number of my own cases. Ultimate results will naturally vary within certain limits, depending upon special groups of cases of sterility and upon the thoroughness with which treatment is carried out. The weight of evidence, all factors considered, points, in the larger series of eventuating pregnancies, to the fact that by relieving tubal obstruction uterotubal insufflation exerts a therapeutic influence in female sterility.

The therapeutic efficacy of uterotubal insufflation may be compared to the results of plastic procedures to restore tubal patency. The analysis of 818 plastic operations reported in reply to a questionnaire sent out by Greenhill is of particular interest in this connexion. There were 54 pregnancies, that is, 6.6 per cent, or 1 pregnancy out of 15 operations. Of these there were 8 ectopic pregnancies, 10 abortions, and 36 live babies, that is, 4.4 per cent successes, or 1 living baby out of 22.5 operations.

Of 438 patients, whose Fallopian tubes showed improvement in patency after a second or third insufflation, 66 became pregnant (15.07) which figure compares favourably with the results obtained after surgical intervention. When diathermy and other methods are added the percentage of success may be reasonably expected to increase as has actually been reported.

Tubal insufflation followed by lipiodol injection. In 7 of the successful cases with high-grade strictures, lipiodol was also employed. In 3 cases insufflation had been done once before lipiodol was employed, in 3 cases 3 times, and in 1 case 4 times. In 4 of these cases insufflation also followed the lipiodol injection, once in 2 cases, 4 times in 1 case, and 7 times in the other before pregnancy ensued.

The therapeutic efficacy of lipiodol in these 7 cases is difficult to appraise, because, altogether, 29 insufflations had been done before or after the 7 single lipiodol injections. I have had occasion to inject lipiodol in 159 patients, and pregnancy followed insufflation and lipiodol in these 7 patients alone. If we omit 99 cases of tubal closure and the 7 cases in which the examination was unsatisfactory, the incidence of pregnancy in the remaining 53 cases is 13.21 per cent. This is less than half the percentage of successes where insufflation alone was employed in the general group of patients having tubal strictures (31.13 per cent).

There are many other items which are of interest but which the limitations of time do not permit discussion. May I in conclusion recall the fact that we are here to consider the merits of uterotubal insufflation and hysterosalpingography. For the diagnosis of tubal patency and non-
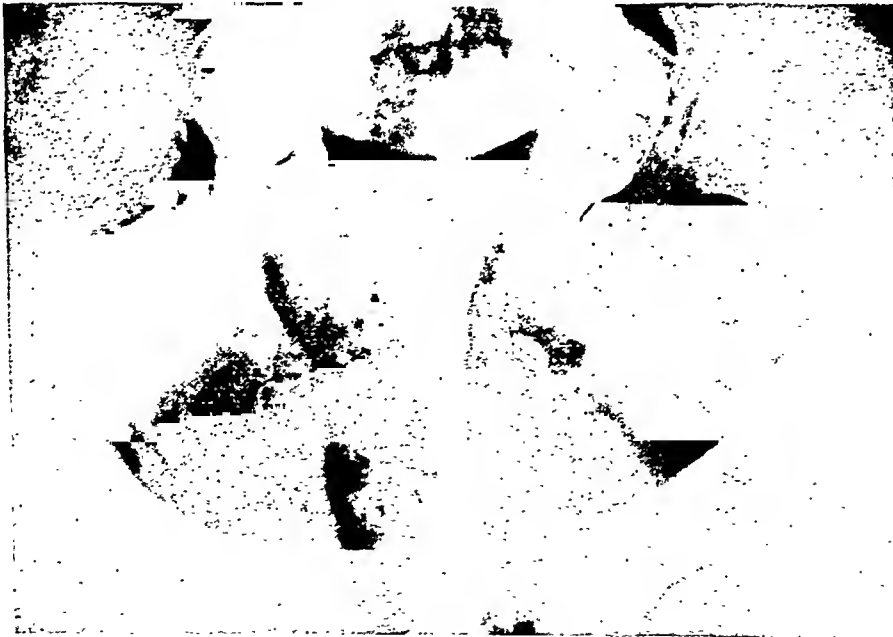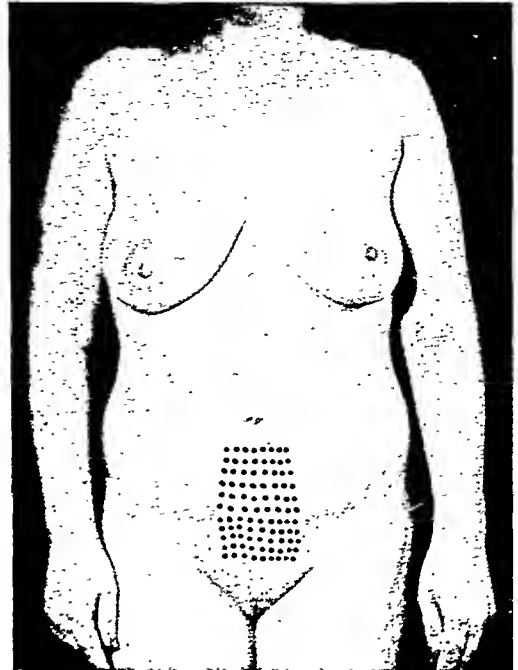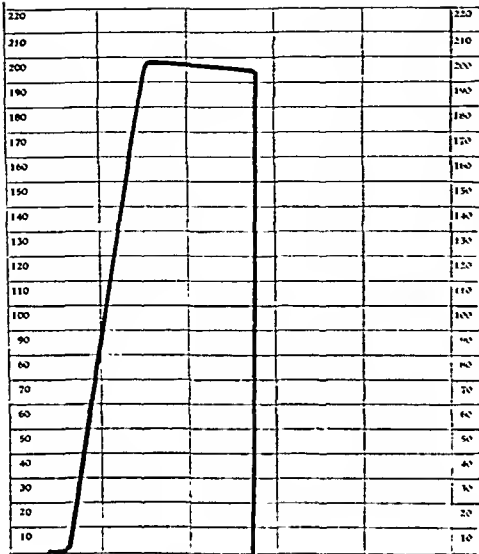
FIG. 2.

Uterotubal insufflation showing bilateral tubal obstruction accompanied by suprapubic pain and hyperaesthesia, indicating bilateral interstitial tubal obstruction. Hysterosalpingogram confirms these findings.

I.C.R.

patency the former has proved the method of choice. For the diagnosis of intrauterine pathology both in sterility and in general gynaecology, hystérography *per se* is invaluable. Its only competition is uteroscopy, which should perhaps be adopted more generally by gynaecologists. From the therapeutic side uterotubal insufflation aids the sterile woman who has partial tubal obstruction. The results exceed those of hysterosalpingography on the one hand and of surgical plastic procedures on the other. When other therapeutic, physical and hormonological adjuvants are added to uterotubal insufflation the salvage may be appreciably improved.

Studies in the Biology of the Cervix and its Relation to Puerperal Infections

BY

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PUERPERAL fever is a clinical entity which has long been recognized. The earliest known reference to the condition in medical literature was attributed to Hippocrates in the 5th century B.C. His teaching was that fever occurring during the first days of the puerperium was due to suppression of the lochia. His influence on subsequent medical thought was of enormous consequence and about 1,500 years passed before his conclusions were seriously questioned.

William Harvey in 1651, stated that "foul and putrid lochia sets up fever and other violent symptoms." He considered the raw placental site as a "vast ulcer" and stated "If any part of the placenta adhere to the uterus the lochial discharges become foetid, green and putrid." These views were a great advance in the study of the aetiology of puerperal infection.

Charles White, of Manchester, in 1773, stated that he thought puerperal fever and surgical fever were similar, and he advocated postural drainage, isolation of infected cases and rigorous cleanliness in combating puerperal fever. His results were so good that many continental teachers visited his clinic, among them Boer of Vienna, who applied White's teaching in his own clinic.

In 1789, Baudelocque suggested that the introduction of the hand into the parturient canal and the use of instruments were factors in the aetiology of puerperal infection, and in 1795 Alexander Gordon stated that puerperal infection "seized women only as were visited or delivered by a practitioner, or taken care of by a nurse, who had previously attended patients affected with the disease."

In 1847, Semmelweis noted a high mortality from puerperal fever among women confined by students who attended post-mortem examinations as compared with a low mortality among women confined by midwives, and concluded that the disease was due to contamination. He reintroduced the principles of White and insisted on the attendants washing their hands in lime water before confining the patients. Later he stated that though infection may be conveyed to the woman by her attendants she may also infect herself owing to retention in the birth tract of material which had undergone decomposition.

In 1879, Pasteur demonstrated the presence of streptococci in the lochia of a woman who died of puerperal fever, and for some time this organism was considered the sole cause of the disease.

In 1883, Ahlfeld revived the problem of autoinfection. He postulated that it was possible that "pathogenic organisms may

exist in the genital tract during pregnancy without giving rise to symptoms, and that they only exert their influence during labour or the puerperium when the wounds which follow labour will afford abundant opportunity for their absorption." Döderlein, in 1887, and Winter, in 1888, found varieties of pyogenic organisms in the vagina and cervix of non-pregnant women (Peckham, 1935; Galloway, 1945).

Harris and Brown (1929) reviewed 113 cases of streptococcal puerperal infection, and concluded that puerperal infection due to aerobic β-haemolytic streptococci were almost invariably exogenous in origin, while γ-non-haemolytic streptococci were usually the cause of endogenous puerperal infections.

Leonard Colebrook (1930) reviewed the position of the streptococcal organisms causing puerperal infections and stated that strictly anaerobic streptococci had been isolated from the blood of a number of cases of puerperal fever and that similar organisms had been found in the vagina during pregnancy. He isolated anaerobic streptococci from the blood of 17 patients with puerperal fever and found in 8 cases the blood culture gave a mixed growth, two types of anaerobic streptococci or anaerobic streptococci and some other organism. The incidence was such that a contagious origin of the infection was unlikely, 10 cases had undergone intra-uterine manipulations during labour. There was a mortality of 39 per cent.

Meleney (1931) discussed the possibility of the adjuvant action of organisms found together in certain disease processes and concluded that the " synergistic action of such bacteria should always be kept in mind in studying disease processes involving tissues, organs, or systems in which mixtures of organisms are frequently or occasionally found."

Douglas and Davis (1946) obtained cultures from uteri in 1,000 patients with puerperal infection. They reported that the majority of organisms found in these cases were also frequently found in the lower genital tract in the pregnant and non-pregnant woman, and considered that these cases represented autogenous infection. They stated that " endogenous infections constitute by far the largest group encountered and also the most difficult to control." They also suggested that the process of infection commenced with the onset of labour, in the great majority of patients labour terminated before clinical signs of infection developed, and that the development of intrapartum infection did not imply that the postpartum course would be febrile or that the patient would be classified as having morbidity by any of the standards commonly employed. They concluded that the incidence of endogenous infections may be decreased by control and restoration of blood loss, limitation and timing of operative procedures, removal of retained portions of placenta at the end of the third stage of labour, early repair of lacerations with proper surgical asepsis and control of intercurrent disease. It will be noted that they emphasized morbidity which may not become manifest till the lying-in period is well over.

Hite, Hesseltine and Goldstein (1947) studied cultures taken from a series of 248 normal and pathological obstetrical and gynaecological patients. They found that the variety of bacteria and the type of bacterial flora were not very different in cultures taken from the postpartum intrauterine cavity of normal and infected patients and from the vagina in trichomoniasis. They stressed the fact that the patients suffered from mild and localized infections and in considering the diversity of bacteria present suggested that there is a probability of synergistic infection. Further they found that the bacterial flora

of the vagina in normal pregnant patients resembled that found in patients with monilial and non-specific vaginitis. The organisms found were grouped as aerobes and anaerobes. The former included *Staphylococcus albus* and *S. aureus*, streptococcus alpha type, haemolytic and gamma type, diphtheroid rods, coliform rods, fungi and aciduric rods. The anaerobes were grouped as facultative, being streptococci and strict anaerobes which included streptococci, micrococci, diplococci, *Bacillus necrophorum*, *B. melaninogenicum*, fusiforms and other bacteroids. It is noteworthy that these authors have investigated conditions likely to cause morbidity rather than conditions likely to lead to mortality.

The role of the vagina and the changes which it undergoes during menstruation and pregnancy have been studied. Papanicolaou (1933) studied the cytology of smears made from fluid withdrawn by a pipette from the vagina at different stages of the menstrual cycle and described the rhythmic changes occurring.

Cruickshank and Sharman (1934) studied the vaginal epithelium at different ages and under different conditions together with the bacterial flora and vaginal pH. They found that the pH became more acid when glycogen was found in the vaginal epithelium and considered the conditions then present as unfavourable for the growth of pathogenic organisms. They specifically noted a great increase in glycogen in the vaginal epithelium in pregnancy and considered that an increase in oestrin was responsible for it; the mechanism being an attempt to kill any pathogenic organisms present or likely to be introduced into the vagina.

An increase in thickness of the vaginal epithelium in pregnancy in Rhesus monkeys was noted by Davis and Hartman (1935), and similar changes were found in

women by Davis and Pearl (1938) as well as postpartum involutional changes. They considered that oestrin causes marked proliferation of the vaginal epithelium with deposition of glycogen and the latter authors postulate that one of the functions of vaginal acidity is to guard against infection of the genital tract during pregnancy, labour and the puerperium.

The role of the cervix as a possible source of puerperal infections has not been studied extensively. Frost (1939) reported a series of 30 patients with cervical erosions and pregnancy. He treated these women by electro-coagulation lightly, searing the portio vaginalis cervicis only and found that healing occurred in 4 to 8 weeks, labour was not prolonged and no patient miscarried. He undertook the treatment because he believed that the inflammatory and infectious process would spread and possibly cause salpingitis, metritis or even pelvic peritonitis. However, he does not appear to have studied the lesions and their progress during pregnancy.

The changes in the cervical mucosa occurring during the menstrual cycle were studied by Woollner (1936, 1937). He described changes occurring in the surface cells, in the glands and in the stroma. After menstruation the surface cells are low columnar with little cytoplasm; as the cycle proceeds these cells become tall columnar, densely crowded and bulging with secretion; during menstruation they are shed and repair occurs from the broken ends of glands. The stroma after menstruation consists of dense fibrous tissue with widely spaced cells whose nuclei almost fill the cells, blood vessels are collapsed. Gradually there is an increase in the number of cells and the stroma becomes oedematous, the cells are larger and blood-vessels engorged till during menstruation haemorrhages occur. The glands after menstruation are scanty, widely scattered

and tubular, lined by low columnar cells. Gradually the glands increase in size and number and become crowded and branching. The cells become high columnar and bulge into the lumen and there is evidence of secretion. During menstruation there occurs extensive destruction and exfoliation of the epithelial elements, some glands being entirely denuded of epithelium. Glycogen was found in all stages of the cycle, in the stroma constantly, but was found in the cytoplasm of the epithelium only just before menstruation. Woollner (1939) also studied the effect of hormones on the cervical mucous membrane and concluded that oestrin alone caused proliferation of columnar epithelium, oedema of the stroma and distended blood-vessels; luteal hormone alone did not affect the gland elements but stimulated the squamous cells which proliferated and invaded the cervical canal. Finally when both hormones were given together both elements were stimulated, the glands becoming racemose with tall columnar cells and the stratified epithelium projecting into the stroma while the superficial layers showed vacuolation and parakeratosis.

Barton and Wiesner (1945) studied changes in the cervical mucus during the menstrual cycle. They state that during the ovulatory phase the secretion is clear, colourless and viscid and while the exterior is acid from contact with the vaginal flora the interior of the cordon of mucus is alkaline. During the luteal phase the flow diminishes in quantity and becomes opaque while remaining viscid and alkaline. This opacity is due to desquamated cervical cells and leucocytes which appear in increasing numbers as the menstrual cycle enters the second phase. These desquamated cells and leucocytes are found in the endocervix of healthy fertile women. They consider that this mucus forms a barrier through which only healthy sperms can penetrate. Infertile women whose cervix is at fault can be grouped as women with " dry " cervices, women with atypical mucus—often a thick plug of mucus—and patients with frank endocervicitis.

Petrowa and Berkowskaja (1935) studied sections of the cervix in 13 patients who underwent operation at varying times from 3½ to 8 months' pregnancy; 6 were primigravidae and 7 multiparae. Further sections were studied from 2 cervices removed during parturition and 4 cervices during the puerperium. They found that the glands and stroma underwent profound changes during pregnancy and parturition, the glands undergoing increasing proliferation, hypersecretion and dilatation as the pregnancy advanced. They noted that squamous metaplasia of the surface and glandular epithelium occurred in 8 cases. The stroma retained its youthful character during pregnancy, the cells being often of a decidual nature and at times a genuine decidual focal reaction was seen. Further they observed that in 1 case of hydatidiform mole the changes were more pronounced. They found an almost complete shedding of the cervical mucosa in the cervices of the 2 parturients in their series. These patients had hysterectomy performed for ruptured uterus and it is permissible to wonder what interference had occurred before operation was performed, causing damage to the cervical mucosa. Finally they found regeneration of the mucous membrane of the cervix uteri and the restoration of the secretory function of the glands accomplished in the first 10 days of the puerperium. They considered the cervical mucosa was restored to its original thickness in 4 to 6 weeks postpartum.

Levey (1936) reviewed the literature and gave a summary of changes occurring in the cervix uteri during pregnancy. He stated that the glands underwent marked

hyperplasia and hypertrophy, they were very active and underwent many trans-formations — corkscrew-shape, dilatation, contortion and some undergo cystic changes. The glands grow down and out-ward often in papillary projections. The epithelial cells may be tall columnar, some are full of mucus. In other areas there may be reduplication of the epithelial cells leading to a double layer of cells. During the 8th month the cervix appears to be almost one mass of mucous tissue extend-ing to the muscle layer. Mucus produc-tion occurs about the beginning of preg-nancy and is very marked at the 3rd month, the mucus often containing round cells and plasma cells. The stroma becomes loose and spongy and the cells appear younger and are clear and swollen. Numerous capillaries are present in the loosely arranged connective tissue which is much diminished in amount and at term only a few delicate supporting fibres are to be seen.

Hofbauer (1933) examined 29 specimens of gravid uteri and noted a variety of epithelial changes. In the majority the changes observed were reduplication of cell layers, vacuole formation and polymor-phism of the nuclei. In 8 cases, however, epithelial proliferation with stratification, occurrence of mitotic figures, epithelial down-growth into the connective tissue and goblet-cell formation were noted. He suggested that these changes might repre-sent an important link in the chain of factors causing later epithelial variations and possibly carcinoma.

The work of several investigators (Over-holser and Allen, 1935; Hisaw and Lend-rum, 1936; Korenchevsky and Hall, 1937, 1938) suggests that metaplastic changes in the cervix uteri may be due to oestrin stimulation and Woollner (1939) and Bourne and Williams (1945) believe that cervical "erosions" are of hormonal origin.

No attempts seem to have been made to study changes in the healthy and diseased cervix during pregnancy and postpartum, nor to assess the part played by patho-logical conditions of the cervix in causing morbidity during the puerperium. While every clinician is familiar with the story of symptoms of pelvic inflammation "ever since my last baby," there are many gaps in our knowledge of the mechanism by which such spread of inflammation occurs.

The present investigation was under-taken in an endeavour to discover if cervical lesions present during pregnancy were caused by or harboured organisms which could spread into the tissues during labour and the puerperium and be respon-sible for the low-grade infections so fre-quently seen in women who have borne children.

MATERIAL STUDIED.

The work was undertaken in the out-patient department of King George V Memorial Hospital for Mothers and Babies. The patients were referred to the Leucor-rhoea Clinic for observation and treatment. Twelve normal patients were investigated; to eliminate any traumatic or infective factor, only primiparae were included. Another series of cases in which the cervix did not appear entirely normal but whose variations did not seem very excessive were classified as "For Observation". They had originally been referred to as "Nor-mals". In this group there were 7 cases. The abnormal patients were grouped as primigravidae, of which there were 37, and multiparae, of which there were 21. It was thought important to study effects of trauma apart from other factors.

TECHNIQUE EMPLOYED.

Each control patient was investigated as soon as possible after pregnancy was estab-

lished. The patients complaining of discharge were investigated as soon as referred to the clinic. The patient was placed in the dorsal position with the knees drawn up and separated. Smears and cultures were collected from the urethra. Then a sterile bivalve-speculum was introduced into the vagina and the cervix and vault exposed. Smears and cultures were taken from the cervix and vaginal vaults. Any collection of pus or matter in the vagina was specially investigated.

In a certain number of cases a sterile swab-stick was rubbed over the vagina and a second over the endocervical canal. The swab-sticks were then gently rolled over 2 glass slides which were exposed to iodine vapour. The slides were then examined, and in all the vaginal smears epithelial cells staining a mahogany colour indicating the presence of glycogen were seen. No such finding was made in the cervical smears. The procedure was very tedious and as it was felt that insufficient knowledge was obtained from a time-consuming practice, it was dropped.

A swab-stick was passed into the cervical canal, then placed in a drop of saline on a palette, and a drop of universal indicator was then added. The resulting colour gave the reading for the cervical pH. The vagina was next washed out with saline, the washings kept for bacteriological study and one drop added to a drop of universal indicator on a palette. The colour-change gave the readings for the vaginal pH.

The vagina was then swabbed out and a biopsy taken from the cervix. At first an attempt was made to curette the cervical canal, but the endo-cervix appears to be too firmly fixed to the underlying tissue for this method to be successful. A change of instrument gave more satisfactory results. A laryngeal punch forceps was used and an attempt made to obtain a specimen from the muco-squamous junc-tion so that the orientation would be easy for the microscopist.

One factor arose in connection with the collection and interpretation of the biopsies that deserves special mention. Collection of suitable biopsy material from normal cases was much more difficult than from abnormal cases. This seems to be a very important point. The external os is more tightly closed in normal cervices than in the pathological cervices.

At subsequent visits the cervix was again inspected and biopsies taken at monthly intervals in normal cases. Care was taken to use a fresh area of cervix at each visit to prevent any spoiling of the microscopic picture with healing phenomena. If it was necessary further investigations were done, such as cultures, collection of saline washings or catheter specimens of urine. Sugar-tolerance tests were also undertaken in patients harbouring monilia or complaining of vulval irritation.

Repeated biopsies were taken in abnormal cases as often as was felt advisable. An endeavour was made in all groups of cases to take biopsies as soon as possible after the confinement and a further biopsy was then taken just prior to discharge. The patients were requested to return at 6 to 8 weeks postpartum and again at 3 months postpartum, when further biopsies were taken. If it was found impossible for the patients to attend they were asked for a report on their condition.

FINDINGS AT THE FIRST VISIT AND BIOPSY STUDIES.

A—NORMAL CASES.

The 12 cases studied proved to have findings similar in most respects to those described as normal in other countries. The age distribution is as follows: only 1 patient was over 30 years; the other 11 were in the 20 to 30 years age group. The pH

findings are tabulated in Table I, and are quite in accordance with other findings. The findings seen in the smears are included in Table II. It will be noted that there were few polymorphs or organisms found in any site in the normal cases. The organisms found are tabulated in Table III. Two patients had monilia present in

During pregnancy the endocervical mucosa and the portio vaginalis undergo profound changes. The earliest change is thickening of the squamous epithelium. Decidual change in the stroma can appear as early as 10 weeks. The glands begin to increase in size and number at about 4 to 5 months. At this period there is evidence

TABLE I.
Comparison of pH Findings.

Site	pH	Normal Total 12	Observation Total 7	Abnormal primigravidae Total 37	Abnormal multiparae Total 21
Vagina	4	6	5	13	5
	5	4	2	8	8
	6	1	—	3	3
	Bleeding	—	—	7	1
	Not recorded	3	—	6	3
Cervix	6	1	—	1	1
	7	1	4	3	4
	8	7	3	21	10
	Bleeding	—	—	8	1
	Not recorded	4	—	5	5

the genital passages, but they did not develop vaginitis and did not complain of irritation and may therefore be considered as carriers. One patient complained of irritation at the 14th week. A sugar-tolerance test revealed a normal blood-sugar curve, but she leaked sugar from the kidney and when she was put on a reduced carbohydrate diet the irritation ceased and she had no further trouble. The macroscopic appearance of the cervix did not alter very much during pregnancy. As the patient entered the 3rd trimester there was often some transudate in the vagina and a small amount of mucus in the os. Two patients had a little heaping of endocervical epithelium protruding through the os, and in 1 case the cervix·was patulous at term.

Biopsy Findings.

All these biopsies were stained with haematoxylineosin.

of secretion and slight hyperplasia of the epithelial cells. At 5 to 6 months the stroma shows a marked increase in vascularity and oedema begins to appear. Goblet-like cells were noticed for the first time, also a syncytial-like arrangement of epithelial cells. At 6 to 7 months the squamous epithelium begins to thin and the stroma decreases in amount, its place being taken by the increase in glands. Squamous metaplasia was noted for the first time at this period. Secretion and hyperplasia are very marked features. The glands assume many shapes—racemose, elongated, dilated and filled with secretion. Nabothian follicles were seen for the first time at this period. These changes progressed to term and in all these cases inflammatory cells did not present a marked feature. When present they were confined to the tips of papillae, the muco-squamous junction, the lumina of glands or Nabothian follicles or mucus bathing the tissues.

TABLE II.
Comparison of Smears.

Site whence taken	Cell type	Number	Normal cases Total 12	Observation cases Total 7	Abnormal primigravidae Total 37	Abnormal multiparae Total 21
Vagina	Epithelial cells	Profuse	—	—	2	—
		Numerous	5	4	20	16
		Moderate	6	2	10	5
		Few	—	1	5	—
		None	1	—	—	—
	Polymorphs	Profuse	—	—	2	—
		Numerous	—	—	9	10
		Moderate	—	—	6	4
		Few	8	7	19	6
		None	4	—	1	1
	Organisms	Profuse	1	2	10	10
		Numerous	5	3	17	10
		Moderate	2	2	7	1
		Few	3	—	2	—
		None	1	—	1	—
Urethra	Epithelial cells	Profuse	—	—	—	—
		Numerous	4	3	13	12
		Moderate	5	4	16	5
		Few	2	—	7	4
		None	1	—	1	—
	Polymorphs	Profuse	—	—	—	—
		Numerous	—	—	—	1
		Moderate	—	—	6	—
		Few	6	3	22	14
		None	6	4	13	6
	Organisms	Profuse	—	—	—	—
		Numerous	—	1	9	4
		Moderate	1	2	15	8
		Few	6	2	1	7
		None	4	2	3	2
Cervix	Epithelial cells	Profuse	—	—	—	—
		Numerous	3	2	4	6
		Moderate	3	3	14	5
		Few	6	2	19	10
		None	—	—	1	—
	Polymorphs	Profuse	—	1	—	1
		Numerous	1	4	19	9
		Moderate	3	2	13	6
		Few	6	—	5	5
		None	2	—	—	—
	Organisms	Profuse	—	—	5	3
		Numerous	1	2	13	6
		Moderate	3	—	11	2
		Few	5	5	7	9
		None	3	—	1	1

TABLE III.

Comparison of Cultures

Organisms	Normal primiparae Total 12			Observation primiparae Total 7			Abnormal primigravidae Total 37			Abnormal multiparae Total 21		
	Cervix	Urethra	Vagina	Cervix	Urethra	Vagina	Cervix	Urethra	Vagina	Cervix	Urethra	Vagina
Non-haemolytic streptococcus	4	2	4	4	3	5	15	15	19	8	8	9
Staphylococcus albus	4	4	3	–	2	1	7	10	8	1	6	4
Bacillus coli	–	–	–	–	–	–	1	3	2	–	–	–
Monilia	2	2	1	1	1	1	8	10	11	9	11	11
Staphylococcus aureus	–	–	–	–	–	–	1	1	1	–	–	–
Bacillus proteus	–	–	1	–	–	–	–	–	–	–	–	–
Diphtheroids	2	3	2	–	–	–	2	5	5	1	1	1
Döderlein's bacillus	1	–	2	–	–	1	2	2	2	2	3	3
No growth	4	4	3	3	2	–	11	10	5	5	4	3
Trichomonas vaginalis	–	–	–	–	–	–	–	–	1	–	–	1

It is perhaps worthy of notice that one patient had fibrous stroma and very few glands right up to term. It was considered possible that her confinement would be long and when she did come into labour she had an instrumental delivery after $74\frac{1}{2}$ hours and her cervix was badly lacerated. The above conclusions are drawn from the following data. In the 12 patients there were 8 biopsies collected under 10 weeks' cyesis. Of these 4 were unsatisfactory. The other 4 cases showed a thickened squamous epithelium. In 3 cases the stroma was of an adult, non-pregnant type; in 1 case there was a patch of decidual reaction. The endocervical epithelium was of columnar type, not secreting and inactive. A few glands were noted in 1 case only. No inflammatory cells were noted.

At 3 to 4 months' cyesis 5 biopsies were unsatisfactory. In the remaining 7 cases the squamous epithelium was thickened, the stroma became more vascular in 3 cases and slightly more oedematous in 4 cases. In 2 cases it remained fibrous. The endocervical epithelium was obtained in 4 cases. In these cases the epithelial cells were in-creasing in height, there was a little evidence of secretion. In 1 case there were a few low papillae. In 1 a few glands of tubular type were beginning to appear. In 1 case only were a few leucocytes noted at the mucosquamous junction.

At 4 to 5 months' cyesis, only 1 biopsy was unsatisfactory. In all the 11 remaining cases the squamous epithelium was thickened. The stroma varied. In some cases there was definite evidence of oedema and increasing vascularity. In 3 others the stroma remained fibrous but showed evidence of increased vascularity. In 4 cases the endocervical mucosa was completely missed. In 2 cases there was a very marked increase in the number of glands. The surface epithelium as well as the glandular epithelium became taller and showed evidence of increasing hyperplasia and secretory activity. In these 2 cases inflammatory cells were seen, numerous in 1 case, a few only in the other. In the remaining 6 cases the surface epithelium was showing evidence of hyperplasia, some reduplication of cells occurred and there were signs of secretion. The glands, while

not numerous, were beginning to increase in size and number. In 2 cases only were a few inflammatory cells noted at the muco-squamous junction.

At 5 to 6 months' cyesis, in 8 cases the squamous epithelium was thickened and in 2 cases it was not seen, in the remaining 2 cases it was only a thin strip. The stroma was fibrous in 3 cases, in 1 case there was a patch of decidual reaction. In the remaining 8 cases the stroma was becoming vascular and oedematous, the dilatation of vessels being the most noticeable feature. In 4 cases the endocervical mucosa was missed. In all the other cases the glands were increasing in number and like the surface epithelium showed evidence of commencing hyperplasia and secretion. Three patients had Nabothian follicles. Goblet-like cells were seen in 2 cases. In 1 case there was a syncytial-like arrangement of epithelial cells. Inflammatory cells were seen in 3 cases; a moderate number around the glands and in follicles in 2 cases, and a few at the mucosquamous junction in 2 cases. No inflammatory cells were seen in 4 cases.

At 6 to 7 months cyesis the squamous epithelium was thickened in 8 cases. In 2 cases it was not seen and was thin in 2 cases. The stroma in 1 case remained fibrous. In all the others it was vascular and oedematous, in 2 cases it was very scanty, being largely replaced by the epithelial elements. The endocervical epithelium was not obtained in 4 cases. Squamous metaplasia was noted in 3 cases. In the other cases the surface epithelium was secreting actively, there was reduplication of the epithelial cells which were very hyperplastic and which were showing evidence of great secretory activity. Nabothian follicles were observed in 3 cases. Some glands were racemose, others elongated; goblet-like cells were noted in 1 biopsy. Inflammatory cells were not seen

in 4 cases. In the remaining 4 cases there were a few leucocytes, both polymorphs and round cells scattered in glands, mucus and at the mucosquamous junction.

At 7 to 8 months' cyesis biopsies were not obtained in 2 cases: In the other 10 cases the squamous epithelium was missed once, was beginning to thin in 2 cases and was thick in the remaining 7 cases. The stroma was vascular, oedematous and scanty in 9 cases, it was fibrous in 1 case. Endocervical tissue was missed in 2 cases. In all the remaining cases the epithelium was very active, marked secretion and hypoplasia occurring, numerous goblet-like cells were seen. Metaplasia was observed twice. Glands were numerous except in 1 case and Nabothian follicles were noted twice. The glands were of many shapes, some racemose, some dilated and some elongated. Inflammatory cells were noticed only once in any marked degree and then they were present in mucus and not in the tissue.

At 8 to 9 months' cyesis biopsies were not obtained in 4 cases. The squamous epithelium was not seen 3 times; it was thin in 2 cases but of the usual pregnancy thickness in 3 cases. In all but 1 case where it was fibrous, the stroma was vascular, oedematous and very scanty. Surface epithelium could only be identified in 4 cases, in 2 of which there was squamous metaplasia. Elsewhere the cells were tall columnar, and actively secreting with goblet cells present, except in 2 cases where secretion was not a marked feature. Glands were a marked feature except in 3 cases. As a rule the tissue looked somewhat spongy and compressible. In 6, no inflammatory cells were seen. In 1 case the distribution was patchy. In 2 cases they were widespread in mucus, at the mucosquamous junction and in the gland lumina.

One biopsy was taken at term. In this specimen no squamous epithelium was

observed. The stroma was vascular and oedematous, and there was a patch of decidual reaction. The glands were racemose and the epithelium continuous with the surface epithelium showed advanced metaplasia, was actively secreting and goblet-like cells were present. No inflammatory cells were seen.

Postpartum Biopsies.

Conclusions are difficult to draw from these biopsies as trauma and interference cannot be eliminated, but it would appear that the greater part of the endocervical mucosa is shed during or immediately after parturition. The stroma begins to become much more cellular and to increase in amount. The cells are at first rounded and become crowded together. Later they become spindled-shaped. The vessels become collapsed and, about the 10th to 14th day, perivascular thickening can be observed. The endocervical mucosa begins to regenerate early, about the 7th day, and reaches a considerably advanced stage by the 14th day. Glands are a variable feature: scanty in some cases, of adenomatous or follicular proportions in others. Metaplasia is a marked feature in nearly half the cases. Inflammatory cells were also variable being present in 9 cases and numerous in 4 cases. They do not appear to be related to trauma, pyrexia or interference.

The basis for the above statement is to be found in the following facts.

Four biopsies were taken within 16 hours of the end of labour. They were all taken from patients who had normal deliveries. Only 1 of these patients had an apyrexial puerperium. The squamous epithelium was thin in 2 cases, missing in 1 and thick in the last. The stroma was oedematous and vascular in all cases, in 2 there was evidence of increase in the number of con-

nective tissue cells which were rounded. There was some pink-staining amorphous material around the vessels in 1 biopsy. Glands were not a prominent feature, their number had decreased and there was no evidence of secretion. Squamous metaplasia was seen in 1 biopsy. Inflammatory cells were widely scattered in 2 cases, 1 of which was pyrexial, the other apyrexial. Few or none were seen in the other 2 cases, both of which had mild pyrexia.

Biopsies were taken from all 12 patients between 7 to 14 days postpartum. One of these was unsatisfactory. The squamous epithelium was missing in 2 cases and was only a thin strip in 3 cases. In the remaining 7 cases it was thick. The stroma showed very great changes. In all cases it had increased in amount and had become much more cellular, the cells being round cells crowded together. In 1 biopsy taken on the 7th day these connective tissue cells were becoming spindle-shaped, but as a rule this change did not occur till the 11th to the 14th day. Perivascular thickening was noted in 4 cases, the earliest day being the 7th. One case where the cervix had been lacerated extravasated blood was undergoing organization on the 9th day. The endocervical mucosa showed various features. It was missed in 2 cases, in 2 only a few broken glands were observed. Papillae were observed in 2 cases, in 1 of which no glands were seen. Few glands of tubular shape were seen in 2 cases. In 5 biopsies the glands were numerous, sometimes racemose, sometimes dilated, on one occasion forming small adenomatous clumps. Metaplasia was observed in 5 biopsies and secretory activity only twice on the 10th and 14th day of the puerperium. Inflammatory cells were a variable feature. They were noted in considerable numbers on 4 occasions, a few only 5 times. In 1 biopsy there was none. There was no relation

between trauma, interference or pyrexia, and the number of leucocytes present.

Biopsies Taken at Return Visits.

The changes which occur in the cervical mucosa during the puerperium appear to continue and reach their maximum about the 3rd month postpartum. Metaplasia was still present and the endocervical elements had reached a resting phase or had formed what amounted to an erosion although this was only evident clinically in 1 case and it was only in this case that inflammatory cells were a marked feature, elsewhere their distribution was patchy and their number small. The stroma had increased in amount and was cellular. Some signs of perivascular thickening persisted. The squamous epithelium had returned to its resting state.

These conclusions were drawn from analysis of the following facts. Biopsies were taken from 8 patients, 5 biopsies were taken 2 months postpartum. The squamous epithelium was missed in 2 cases, cut on the skew in 1 and of pre-pregnancy thickness in the other 2 cases. The stroma was increased in all with some round spindle-shaped cells usually crowded together. One biopsy showed marked perivascular thickening. In 2 cases there were few glands continuous with the surface epithelium and secretion was not observed. In 2 other cases the glands were racemose or tubular and fairly numerous, there was no secretory activity, 1 had advanced metaplasia widespread in glands and on the surface. The remaining case developed an erosion and salpingitis. Here there was very marked secretory activity, goblet-like cells were observed and marked metaplasia. Except in this last case inflammatory cells were not a marked feature.

There were 6 biopsies collected 3 months' postpartum. Of these 1 was unsatisfactory.

The squamous epithelium was missed twice. In the others it was somewhat thicker than in the resting state. The stroma had increased in amount and was very cellular in all. There were patches of oedema in papillary tips. In 1 case no glands were seen but in all the others the glands had increased in number and were racemose and continuous with low papillae. The cells were columnar and often the growth was so marked that the microscopic picture suggested a mixed papillary and follicular erosion. In the case that developed a clinical erosion and salpingitis there was very marked secretion. Metaplasia was observed once. Inflammatory cells were either scanty or not observed.

Two biopsies were taken at 4 months' postpartum. There were no changes from the features described under 3 months' postpartum findings.

One biopsy was taken at $6\frac{1}{2}$ months postpartum. In this case the squamous epithelium was missed, there was a moderate amount of stroma which was very cellular and was slightly vascular. There were numerous elongated glands continuous with papillae forming an erosion. The cells were tall columnar, and there was slight secretory activity. No inflammatory cells were seen.

B—OBSERVATION CASES.

The next group to be studied are the 7 cases referred to the clinic as normal. The appearance of the cervix at their first attendance, however, showed a variation from the strict standards adopted while not being definitely pathological. They were, therefore, classified as " For observation ". The age-distribution of all the group was between 21 and 30 years. The pH findings are seen in Table I, and show no deviation from those seen in the normal cases. The findings seen in the smears are included in Table II. Here again the results agree

with those seen in normal cases. The organisms found are tabled in Table III. There was I patient with monilia at the first visit. She developed a mild vaginitis which was readily controlled. A second patient developed monilia during her pregnancy at 4 months, which also yielded readily to treatment. Sugar-tolerance tests were done on both these patients. Both had a glycosuria but a normal sugar-curve. A reduced carbohydrate diet helped to control the condition. The appearance of the cervix at the first visit of these patients is as follows: 2 had appearances suggestive of early erosion, 3 had a reddening around the cervical os and 3 had some slight mucoid discharge.

Progress During Pregnancy.

The 2 patients who developed a monilial vaginitis had a slight mucoid discharge during the entire pregnancy and both had at first visit a fine white veil over the vagina. One developed a small erosion about $\frac{1}{4}$ inch in diameter around the os. This yielded readily to 4 applications of penicillin-sulphanilamide powder given twice weekly. The other patient developed definite cheesy deposits in the vaginal vault. Her cervix remained quiescent. The monilial vaginitis yielded to 4 applications of penicillin-sulphanilamide powder. Two of the patients had reddening around the cervix and mucoid discharge. The lesion did not advance but Nabothian follicles developed during the pregnancy at 24 weeks in I case. The remaining 3 cases all developed erosions. In I the erosion appeared about $\frac{3}{4}$ inch diameter at 15 weeks, in the 2nd the erosion appeared about $\frac{1}{2}$ inch in diameter at 19 weeks and in the 3rd an erosion about I inch in diameter appeared at term.

Antepartum Biopsies.

There is a decided change in the pattern of development exhibited in these biopsies during the course of pregnancy. The squamous epithelium and stroma show the same features. The difference is in the glands. It is also noteworthy that these biopsies were easier to collect and there were fewer failures—3 only—to obtain suitable material. As early as 3 to 4 months cyesis there were papillae and numerous glands present. In 2 cases they were grouped together in adenomatous-like masses. Secretory activity was already obvious in 4 cases. Squamous metaplasia was observed in I case.

At 4 to 5 months metaplasia was widespread in 2 cases and goblet-like cells were visible in 2 cases. In all, the glands and papillae were very much more numerous than in the normal cases, the appearance being microscopically that of adeno-papillary erosions. The glands were distended in I case. Secretory activity was marked in all.

At 5 to 6 months these changes had increased. Metaplasia was observed 3 times, goblet-like cells were a marked feature in 5 biopsies and distended glands were noted 3 times.

At 6 to 7 months the secretory and proliferative activity of the surface epithelium and the glands had increased further. Metaplasia was widespread in 2 cases, adenomatous masses of glands were seen in I biopsy and marked dilatations of glands with flattening of cells was observed in I case. Thereafter the changes increased to term and the resemblance to the normal became more marked at term. Inflammatory cells were not a marked feature. When present they were to be found in mucus, in gland lumina, in the vessels and at the mucosquamous junction. In the whole series of 37 slides they were not seen 8 times, a few only 21 times and in any number in restricted localities, such as at the mucosquamous junction, in the tips of papillae,

in gland lumina, in mucus and around areas of metaplasia only 8 times.

Postpartum Biopsies.

There were 3 biopsies collected at 30 to 36 hours postpartum. In all these, unlike the normal cases, the endocervical epithelium was found persisting in an active secreting condition. The stroma was becoming slightly more cellular and Nabothian follicles were observed in 2 biopsies. A few scattered inflammatory cells were noted in all.

The biopsies taken prior to discharge were taken at intervals of 7 to 19 days postpartum. The stroma had increased in amount and in cellularity. There was marked perivascular thickening in all. Evidence of breaking down of squamous epithelium and endocervical glands and surface epithelium was observed in 4 cases. The areas which were undergoing this change were loaded with polymorphs which in some cases were lying among the squamous cells. The dates of this breakdown were 9, 14, 8, and 8 days postpartum, respectively.

One biopsy taken at 7 days postpartum showed as the only recognizable postpartum signs, increase in stroma due to cellular multiplication and perivascular thickening. The endocervical tissue was still active. Metaplasia was present and inflammatory cells were present around the metaplastic cells.

Another biopsy taken at 9 days postpartum had a resting type of squamous epithelium. The stroma was cellular, the cells being chiefly round cells and slight perivascular thickening was observed. The glands were compact, the cells columnar, showing slight secreting activity. Numerous polymorphs were present on the surface and in gland lumina.

The last biopsy was collected from a patient who had toxaemia on the 19th day postpartum. The squamous epithelium was in the resting stage, the stroma was increased in amount and very cellular, the cells being chiefly spindle-shaped. There was marked perivascular thickening. There were 2 patches of squamous metaplasia on the surface, elsewhere these cells were moderately tall and not secretory. There were a few racemose glands lined by inactive cells. Inflammatory cells were not a marked feature.

It would therefore appear that the factor causing a marked hyperplasia of the endocervical mucosa apparently persists for at least a week postpartum. The thickened tissue is then shed and its shedding is accompanied by an intense inflammatory reaction. This feature was not seen at all in the normal cases. The only case where forceps were used showed this interesting persistence of thickened epithelium and its shedding at 14 days postpartum.

Follow-up Biopsies.

These are best studied in 2 groups, those whose cervices appeared normal clinically and those who developed erosion and salpingitis. Two of the first group of patients had microscopically an inactive follicular and papillary erosion, 2 others had inactive endocervical mucosa resembling that seen in normal cervices. One had a microscopically active follicular erosion. Metaplasia was seen in 1, 11 weeks postpartum. Inflammatory cells were not observed in 3 cases and a few only in 2. Perivascular thickening was very obvious in 1 of the inactive cases.

Two biopsies were taken from each of the patients who developed erosions and salpingitis. In both the stroma had become very cellular and in 1 there was marked perivascular thickening. There was a very marked papillary and follicular erosion in 1, the cells were not secreting and no in-

flammatory cells were observed. In the other there were only a few inactive glands but numerous polymorphs at the muco-squamous junction. At 10 weeks post-postpartum in 1 case the only changes to be observed were increase in secretory activity and inflammatory cells in the tips of the papillae. In the other case the changes noted at 14 weeks postpartum were an actively proliferating papillary and follicular erosion, there was no evidence of secretion but there were numerous polymorphs in the vessels and in papillae.

It would appear from this study that these cases which were grouped separately on microscopic appearances were definitely of a different type to the normal cases. They showed a far greater and an earlier response to pregnancy changes than did the normal group, their endocervical mucosa was maintained for a much longer interval after labour and its breakdown was accompanied by an intense inflammatory reaction and the 2 patients who developed salpingitis had no other causal factor but the presence of an antepartum erosion. From the microscopical findings they may be classified as hyperplastic. They may go on to definite erosions of a type to be described later as "Mixed."

C—ABNORMAL PRIMIGRAVIDAE.

In this group there were 37 cases. Their age distribution is: 6 in the group 17 to 20 years, 29 in the 21 to 30 years' group; and 2 in the 31 to 35-years' group. The pH findings are recorded in Table I. They have been disappointing, no clue to the conditions being found in them. It should be noticed that in 7 cases it was impossible to record the vaginal pH and in 8 cases the cervical pH, due to bleeding from the cervical lesion. The findings in the smears are set out in Table II. It is noteworthy that in the vaginal and cervical smears there

are proportionately more cases showing an increase in polymorphs and organisms than were observed in the normal and observation or hyperplastic groups. The organisms cultured are tabulated in Table III. There is to be observed a greater variety of organisms. Only 1 patient had a trichomonas vaginalis vaginitis. Twelve patients had a monilial vaginitis. Six patients were monilial carriers and did not develop a vaginitis.

The lesions seen at the patient's first attendance are set out in Table IV, 19 patients had acute cervical erosions, 10 of

TABLE IV.
Lesions Seen at Patient's First Attendance

			Abnormal primigravidae	Abnormal multiparae
Cervical erosion	Acute	Large	10	2
		Small	9	1
	Subacute	Large	5	6
		Small	7	0
Chronic cervicitis			3	8
Laceration of cervix			0	7
Cervical ulcer			1	0
Vaginitis			15	8
Vulvitis			4	3
Perineal warts			1	0
Urethritis			—	1
Salpingitis			1	0

which were large and 9 were small. Twelve had subacute erosion, 5 of which were large and 7 small. Three patients had chronic cervicitis. One patient had a cervical ulcer on the dorsal surface of the cervix. Fifteen had vaginitis, 4 vulvitis, 1 perineal warts and 1 salpingitis. It will be realized that some of the lesions were multiple.

The duration of symptoms is set out in Table V. It was not recorded in 4 cases, not noticed in 5 cases. Four patients complained of discharge since the menarche, 6 had had trouble "for years", 6 had suffered an attack before the onset of cyesis. Two dated their symptoms from the onset

TABLE V.
Duration of Symptoms.

Duration of symptoms	Abnormal primigravidae	Abnormal multiparae
Since menarche	4	1
" For years "	6	0
One attack before present cyesis	6	2
Since previous cyesis	0	8
Since onset of present cyesis	2	2
For 1–3/52 of present cyesis	3	3
For 1–2/12 of present cyesis	6	5
For 2–3/12 of present cyesis	1	0
Not recorded	4	0
Not noticed	5	0

of the pregnancy. Three patients had noticed discharge from 2 to 3 months of cyesis. At least half the patients, therefore, entered into their pregnancy with cervical disease.

BIOPSIES.

These patients can be grouped for purposes of biopsy study into 6 groups. They were referred to the leucorrhoea clinic for treatment of discharge occurring during pregnancy, this explains the first 3 groups.

Group 1. Patients with Normal Cervices and Vaginitis.

There were 6 cases in this group. Five had a monilial vaginitis and 1 a trichomonas vaginalis vaginitis.

Their biopsy findings were quite in accordance during pregnancy, postpartum and at return visits with what was seen in the normal group except that the patient with a trichomonas infection had a very marked decidual reaction persisting throughout the course of her pregnancy.

Group 2. Patients with " Observation " or Hyperplastic Cervices and Vaginitis.

There were 2 patients in this group. Both had a monilial vaginitis.

The biopsy findings were the same as those recorded in the " Observation " or

C

hyperplastic group throughout pregnancy, the puerperium and the postnatal period, except that there was an increased inflammatory reaction and many more polymorphs.

Group 3. Patients with a Vitamin-Deficiency Lesion.

There was only 1 patient in this group. She had a non-specific vaginitis and ulcer on the portio vaginalis cervices. The lesions cleared rapidly with parenteral vitamin B administration and did not recur. The cervical biopsies were of the normal type.

Group 4. Patients with a Proliferating Type of Cervical Lesion.

There were 12 patients in this group; 3 had monilial vaginitis as well.

It must be remembered that the changes seen in the normal cases run *pari passu* with the features described below. There was a marked overgrowth of glands and papillae throughout the pregnancy. The cells, however, did not begin to secrete till the normal time—4 to 5 months—about this period, too, reduplication of epithelial cells was first noted. Squamous metaplasia and goblet-like cells appeared about the 6th month. The glands became distended about the 7th month. In all cases, however, inflammatory cells were a very marked feature, especially in the tips of papillae, around glands, at the mucosquamous junction and around areas of metaplasia.

The glands tend to persist even in biopsies collected within 40 hours of confinement, though there may be areas of desquamation of the mucosa with a marked inflammatory reaction. Within 10 to 14 days postpartum there is a papillary erosion reforming, but there is little evidence of secretion, and inflammatory cells, chiefly polymorphs, are numerous. The micro-

scopical evidence of a papillary erosion persisted as long as the cases were followed, even if there was no clinical evidence of cervical erosion. Secretion was not a marked feature.

Group 5. *Patients with a Secreting Type of Cervical Lesion.*

There were 8 cases in this group. Vaginitis was not observed in any of them.

Again the general trend of changes follows the normal pattern. In this group papillae were absent or very low while glands were racemose and did not become elongated to any very marked degree. However, there was evidence of secretion as early as 2½ months, and widespread metaplasia may occur at the same time. Goblet-cells were noted at 3½ months. The glands may become distended with secretion and form larger and more numerous Nabothián follicles than was observed in the normal cases; or they may become filled with a honeycomb of metaplastic cells. Inflammatory cells vary in number and type. Where there is much mucus polymorphs are found in great quantities, these cells are also seen in gland lumina, in papillae, around areas of squamous metaplasia in much greater numbers than were seen in normal or hyperplastic cervices.

Up to 40 hours postpartum biopsies show very marked sloughing of the mucosa with areas of haemorrhage and an intense inflammatory reaction. Some glands and areas of metaplasia persist. From 7 to 14 days postpartum there is usually definite evidence of regeneration with a tendency to formation of a follicular type of erosion but little secretion is seen. At return visits biopsies showed persisting metaplasia, follicular erosion and inflammatory cells around metaplastic areas in glands and at the mucosquamous junction. Secretion was more commonly seen than in the proliferative lesions.

Group 6. *Patients with a Proliferating and Secreting or Mixed Type of Cervical Lesion.*

There were 8 patients in this group, 3 of them had monilial vaginitis.

The biopsies in this group showed features of both the preceding groups throughout the entire period they were under observation. Some cases tended to the proliferating group, others to the secreting group. All stages from the one to the other were seen.

D—ABNORMAL MULTIPARAE.

In this division there were 21 cases. Their age distribution is as follows: Only 1 was under 20 years, 12 were between 21 and 30, 6 were between 31 and 35, and 2 between 36 and 40 years. The pH findings are recorded in Table I. They, like those of the abnormal primigravidae, were not helpful in elucidating the problem. Bleeding prevented a record being taken in only 1 case.

The findings in the smears are set out in Table II. They, like those of the abnormal primigravidae, show a greater number of polymorphs and organisms in cervical and vaginal smears than was noted in the normal and " observation " primigravidae. The organisms cultured are to be found in Table III. Only 1 patient had a trichomonas vaginalis infection. Four patients were monilial carriers and did not develop a vaginitis while 8 patients had monilial vaginitis.

The lesion seen at the patient's first attendance are set out in Table IV. Three patients had acute cervical erosion, 2 of which were large and 1 was small. Six patients had large subacute erosions. Eight patients had chronic cervicitis, 7 had large cervical laceration. Eight patients had vaginitis, 3 had vulvitis and 1 had urethritis. It will be realized that most patients had multiple lesions.

The duration of symptoms is set out in Table V. One patient had had trouble since the menarche. Two had had an attack before the present pregnancy. Eight patients stated their symptoms were first noticed at the onset of the present cyesis and 8 said symptoms first developed during the present pregnancy. Half the patients, therefore, had definite evidence of a cervical lesion before pregnancy began. Ten patients only noted their symptoms during the present pregnancy. However, from inspection of the cervix only 3 patients appeared to have a genuinely acute condition. Most of the lesions appeared to be an acute exacerbation of a chronic condition.

BIOPSIES.

In this subdivision all the patients had a cervical lesion and they, therefore, fall into 3 groups.

Group 1. *Patients with a Proliferating Type of Cervical Lesion.*

There were 4 patients in this group. One had an acute lesion. The other 3 patients had evidence of old " cervicitis ". Two had monilial vaginitis.

The biopsy findings did not differ from those seen in the abnormal primigravidae cases.

Group 2. *Patients with a Secreting Type of Cervical Lesion.*

There were 6 patients in this group. Three had a monilial vaginitis and 1 had both a monilial and trichomonas vaginalis vaginitis. Five patients had big cervical lacerations and 1 had evidence of long-standing " cervicitis ".

The biopsy findings were the same as those noted among the similar group of abnormal primigravidae.

Group 3. *Patients with a Proliferating and Secreting Type of Cervical Lesion.*

This was the largest group, comprising 11 patients. Two patients had a monilial vaginitis. Three patients had an acute cervical condition. Two patients had large cervical lacerations and 6 had evidence of long-standing " cervicitis ".

The biopsy findings were the same as those observed among the similar group of abnormal primigravidae.

Squamous Metaplasia.

So much has been written on the possibility of squamous metaplasia in the cervix being the forerunner of squamous-cell carcinoma that a word must be said about this. From the description of the changes in the pregnant and post-partum cervix it is obvious that metaplasia of varying degrees is a normal occurrence. It is seen in all groups of cervices—normal, observation or hyperplastic, and abnormal. It occurs at an earlier stage in the abnormal cervices and is more widespread probably because glandular proliferation is a more marked feature. Areas of squamous metaplasia are frequently surrounded in the abnormal cervices by inflammatory cells, chiefly polymorphs but sometimes by round cells in the more chronic cases. As seen in these biopsies the change is quite benign and does not appear to have any malignant tendencies. While the various staining methods used by Carmichael and Jeaffreson (1941) were not employed all the various types of metaplasia they describe have been observed. Similar findings are also recorded by Hofbauer (1933) who was inclined to believe that these changes may be the possible starting point of a carcinoma. Auerbach and Pund (1945) believe that a common parent cell may give rise to a metaplastic or a frankly carcinomatous cell. Carmichael and Jeaffreson

(1941) are inclined to the view that the two conditions are not related. From a study of the biopsies taken in this investigation, and from a correlation with sections taken from cervices of non-pregnant patients removed at operation in the gynaecological service there would appear to be a profound difference between this type of cell change and that seen in early cases of carcinoma *in situ*.

Decidual Reaction.

A special comment on this finding must be made before leaving the description of the biopsies. It was observed in 2 normal cases, once at 10 weeks' cyesis and again for the first time at 20 weeks. It was last observed at 38 weeks' cyesis. It was noted once at 29 weeks' cyesis among the "Observation" or hyperplastic group. The condition was noted in 10 abnormal primigravidae. The earliest period at which it

occurred was taken at 12 weeks' cyesis. The latest biopsy in which it was observed was taken at 14 hours after confinement. The only suggestion offered to account for this marked increase in the abnormal cases is that the external os is more patulous in the abnormal groups and that therefore it is easier to take a biopsy higher up the cervical canal where, according to Petrowa and Berkowskaja, decidual changes are more likely to occur.

E—REVIEW OF BACTERIOLOGICAL FINDINGS.

Bacteriological findings of cultures from cervix, vagina and urethra are set out in Table VII. It will be noted that in agreement with other observers (Hite, Hesseltine and Goldstein, 1947; Bryce, 1928) a wide range of organisms has been recovered, and of these the commonest is the non-haemolytic streptococcus. The com-

TABLE VII.
Comparison of Haemoglobin Values During Cyesis.

Trimester	Hb.	Normal Total 12	Observation Total 7	Abnormal primigravidae Total 37	Abnormal multiparae Total 21
	per cent				
	90–100	3	1	6	2
First	80–89	3	1	15	8
	70–79	4	4	13	2
	60–69	—	1	1	2
	90–100	—	—	1	2
Second	80–89	2	—	4	3
	70–79	—	1	6	4
	60–69	—	—	—	—
	90–100	1	—	3	—
Third	80–89	8	4	14	7
	70–79	2	3	15	5
	60–69	1	—	3	2

was observed was 14 weeks' cyesis and in 1 case it was found in a biopsy taken 15 hours after confinement. It was observed in 10 cases among the abnormal multiparae. The earliest biopsy in which it

plete absence of the haemolytic streptococcus is noteworthy and *S. aureus* was recovered only once. While the whole range of organisms was recovered in the normal group, the total number of colonies

on the culture plates was usually low and the presence of the non-haemolytic streptococcus was as frequent as in the abnormal group. The significance of the findings is difficult to assess, since all the bacteria found are commonly considered non-pathogenic in these situations.

The isolation and maintenance of the normal lactobacillus proved unexpectedly difficult, and it was constantly noted that while stained smears from the vagina revealed organisms present by tens and hundreds, the colonies on the plates incubated aerobically were to be counted in units and tens. Two possibilities presented themselves to account for this—firstly inadequate methods of cultivation, and secondly the presence of some antibacterial or inhibitory agent soluble in the secretions. Attempts were made to get over this by introducing a series of culture media, and incubating them under anaerobic and aerobic conditions. These were desoxycholate citrate agar, tartaric acid agar, acetic acid broth, liver digest broth, penicillin broth 10 u/ml. and media containing sheep or human or horse blood. Apart from a single isolation of *Clostridium welchii*, these did not provide any additional information.

Saline vaginal washings were seitz-filtered and added to culture medium, and compared with cultures on plates without such addition, but no effect could be demonstrated. The fact that oestrin preparations are suspended in oil made it impossible to work with them *in vitro* for a similar purpose.

The clinical picture of monilial vaginitis was always confirmed by recovery of *Monilia albicans* in culture, while 2 of the normal patients proved to be carriers of that organism.

The question of synergism between organisms of the normal flora and parasitic invaders is a thorny one and no evidence

had been obtained in this study to suggest a line of attack which might prove profitable.

F—REVIEW OF ANTENATAL TREATMENT.

It is a truism that treatment depends upon cause. Where the cause is known it is actively treated. In these cases the only definite known causes were the vaginal infections caused by monilia and *T. vaginalis*.

Trichomonas Vaginalis Vaginitis.

. One primigravida had an uncomplicated trichomonas infection. She was given stovarsol vaginal compound tablets, one night and morning and was speedily cured.

One multipara had *T. vaginalis* and monilial infection as well as a cervical lesion. She was under treatment at term, having been given stovarsol and the treatment described below for monilial vaginitis.

Monilial Vaginitis.

It must be remembered that only 5 patients had an uncomplicated vaginitis. The others all had cervical lesions, so that often treatment was directed at this condition as well. Further, many patients were referred just before term when it was impossible to judge of cure. The lines on which treatment was given are discussed in a previous paper by one of us (McIlrath, 1946). Glycosuria was found to be an aggravating factor in 19 out of the 21 cases with monilial vaginitis and these patients were put on a reduced carbohydrate diet. It was also borne in mind that infection may come from the bowel and the patient was advised to change her drawers and body-towel daily and boil them to destroy the organisms. More recently it has been the custom to order 20 g. of sulphaguanidine in the hope of preventing reinfection from the bowel. Only 3 cases in which this

was tried are included in this series, in 2 the condition was cured, in the remaining 1 the patient was still under treatment at term. Merthiolate suppositories as described in the paper quoted above were used in combination with other forms of treatment on 11 patients. It was found necessary to use gentian violet paintings 2 or 3 times weekly for 3 patients. This was usually a last line of attack. When this investigation was first started only sulphonamides were available to clear the cervical condition. They were used on 4 patients with monilial vaginitis, and in 3 of these cases in combination with a reduced carbohydrate diet, vitamin-therapy and methiolate suppositories they were successful, while in the 4th case it was found necessary to add gentian violet paintings. When penicillin-sulphanilamide powder became available it was found that the cervical lesions cleared much more rapidly and strangely enough the vaginitis did so as well. Three patients were cured by application of penicillin-sulphanilamide powder and a reduced carbohydrate diet, 1 when vitamin therapy was added, and another 1 when sulphaguanidine was added as well. Two patients required the powder, diet, vitamins and merthiolate suppositories. Thirteen patients at term were still under treatment with various combinations of these five.

Treatment of Cervical Conditions.

In the patients who had no vaginitis and no definite known cause for the cervical lesion the problem was different. It was assumed that two factors were involved, one a hormonal factor, the other an infection superimposed on the macroscopic and microscopic changes occurring in the cervix.

The first effort was directed at removing any infection that might be present. At the onset of the investigation only sulphathia-

zole was available and this was used in 5 cases. Later a supply of penicillin-sulphanilamide powder was made available. It was applied in the out-patient department by an experienced sister. A sterile speculum was inserted into the vagina, the cervix was exposed and a thick coat of the powder was blown on to the lesion by means of a Wyeth insufflator. The treatment was given twice weekly for 2 weeks before the clinician saw the patient again, when it was repeated or not depending on the condition of the lesion. If the lesion appeared to be "healing" and the discharge lessening and becoming mucoid instead of purulent it would be suspended. If there was any doubt, especially near term, or if the findings were unaltered the treatment was repeated. It is amazing to see how these lesions improve clinically with this treatment. Microscopically inflammatory cells disappear or diminish in number in a remarkable manner, thus suggesting that a very important secondary factor is infection.

Unfortunately it was impossible to undertake any hormonal estimations on these patients, so it was decided to use them as "guinea-pigs" and see how they responded to treatment.

Cervical lesions described by Hisaw and Lendrum (1936) and Overholser and Allen (1935) resembling those seen in these patients were caused by massive doses of oestrin, so on 17 occasions various preparations of luteal hormone were employed in dosage of 5 international units twice weekly for 4 weeks in an endeavour to restore hormonal balance. Results were quite disappointing. It was decided to try oestrin, so 10,000 international units of oestroform were given twice weekly for 4 weeks to 8 patients. No untoward effects were observed but there was no improvement in the cervical condition. The only other hormone preparation used was

Antuitrin "S" (anterior pituitary-like principle obtained from human pregnancy urine) in dosage of 1 ml. (100 I.U.) twice weekly for 2 weeks. It was used on 2 patients without any effect on the cervix. It was therefore decided that direct hormone-therapy was of little avail especially as hormone-assays could not be used to check dosage and drug.

Recent clinical and laboratory work (Biskind, Biskind, and Biskind, 1944; Singher, Kensler, Taylor, Rhoads and Unna, 1944; Segaloff and Segaloff, 1944; Engel and Rosenberg, 1945; Koref and Engel, 1946), however, suggests that the liver inactivates oestrin when the subject is taking a diet containing an adequate amount of vitamin-B complex. It was felt that the administration of the B-complex might help to inactivate excessive amounts of oestrin and so perhaps hasten a return to normal in the cervical condition. As absorption of this complex may be poor when the patient is suffering from a B-avitaminosis, parenteral administration was given in bad cases or at the commencement of treatment in doses of 10 mg. Vibex thrice weekly. Later, or in less severe cases, Vibex 18 mg. daily was ordered by mouth. It was combined with potantol* mv thrice daily to provide vitamin A, hoping this would help to combat infection.

At a result of treatment along these lines the following results were obtained:

Appearance of cervix at term	Multiparae	Abnormal primigravidae	Observation primigravidae	Normal primigravidae
Clinically healthy	4	11	4	12
Clinically not cured	4	8	3	—
Clinically improved	13	18	—	—
Total number	21	37	7	12

* 1 ml. (m. 17) contains vitamin A 16,000 international units, and vitamin D, 2,000 international units.

G—Labour, Puerperium and End Results.

In order to assess the part played by these lesions in causing low-grade pelvic infections it is necessary to review the patient's general health, any complications that may have occurred during pregnancy and labour, the nature of labour, its duration, any trauma that may have occurred, any interference that may have been undertaken, and the nature of the puerperium. These findings are set out in Table VI.

General Health.

The haemoglobin-percentage is taken as an index of the patient's general condition and these readings are set out in Table VII. Three patients in the normal group had values below 80 per cent in the 3rd trimester of pregnancy, 2 patients had values below 80 in the observation or hyperplastic group and the finding was not recorded once. Among the abnormal multiparae the haemoglobin-value was not taken in 4 cases and was below 80 in 7 cases. Hence approximately one third of all the patients were "below par" at the onset of labour.

Complications.

These were rare. Toxaemia occurred once each in the normal group, the observation group, the abnormal primigravidae and the multiparous patients. There was 1 patient who had bronchiectasis and a patent *ductus arteriosus,* another who had a definite vitamin-B deficiency and a third who had a severe anaemia. These 3 patients were in the abnormal primigravidae group.

Type of Labour.

In the normal group 3 patients had instrumental deliveries and all 3 had

o

TABLE VI.

	Hb per cent in 3rd trimester	Complications	Condition of cervix at last prenatal visit	Duration of labour in hours	Nature of delivery	Condition of perineum	Puerperium	Pelvic condition at last postpartum visit	Date of last postpartum visit
NORMAL CASES									
J B.	88	—	Healthy	13	Normal	Intact	Febrile	Report by letter—premenstrual backache	6/12
E.C.	89	—	Healthy	11¾	Normal	Lacerated	Febrile	Cervical laceration	6½/12
E.C.	77	—	Healthy	68	Instrumental	Lacerated	Febrile	Failed to report	
J.L.	89	—	Healthy	11¾	Normal	Lacerated	Afebrile	Report by letter—had retroversion—feeling well	6/12
D.McF.	85	—	Healthy	11½	Normal	Intact	Febrile	Lacerated cervix—salpingitis	3/12
B.O.	98	—	Healthy	11½	Normal	Intact	Febrile	Normal	3/12
T.O.	80	—	Healthy	42	Normal	Intact	Febrile	Failed to report	
L.T.	89	—	Healthy	14	Normal	Intact	Febrile	Cervical erosion—salpingitis retroversion	4/12
E.W.	88	—	Healthy	4	Instrumental	Intact	Afebrile	Normal	2½/12
M.I.W.	76	—	Healthy	74½	Instrumental	Intact	Afebrile	Cervical laceration	3½/12
M.P.W.	81	Toxaemia	Healthy	69½	Instrumental	Lacerated	Afebrile	Cervical laceration	4/12
D.M.	76	—	Healthy	11½	Normal	Lacerated	Febrile	Normal	4/12
OBSERVATION CASES									
E.C.	84	Pre-eclampsia	Healthy	6½	Normal	Lacerated	Febrile	Normal	4/12
M.F.	74	—	Healthy	7½	Normal	Intact	Afebrile	Normal	3½/12
E.F.	83	—	Healthy	13	Normal	Intact	Febrile	Normal	3/12
E.J.S.	88	—	Healthy	9	Instrumental	Lacerated	Febrile	Normal	3/12
K.M.	78	—	Eroded	17¾	Normal	Intact	Afebrile	Subacute salpingitis	4/12
A.W.	81	—	Healthy	23¾	Normal	Intact	Afebrile	Normal	3/12
J.W.	?	—	Eroded	10½	Normal	Intact	Afebrile	Acute cervical erosion—salpingitis	5/12

PHOTOMICROGRAPH 1 (Z4568)

Biopsy of cervix of normal primigravida 10 weeks cyesis. Note thickening of squamous epithelium, increasing vascularity of stroma. Glands not prominent, slight secretory activity.

PHOTOMICROGRAPH 2 (AA820)

Biopsy of cervix of normal primigravida 18 weeks cyesis. Note that glands are increasing in number and activity.

PHOTOMICROGRAPH 3 (AA2096)

Biopsy of cervix of normal primigravida 26 weeks cyesis. Note presence of oedema in stroma, goblet cells and metaplasia.

M. B. McI.

PHOTOMICROGRAPH 4 (AA1974)

Biopsy of cervix of normal primigravida 34 weeks cyesis. Note scanty stroma with marked increase in vascularity and oedema. Increase in number of glands with crowding and reduplication of cells, a syncytial-like arrangement at times and metaplasia.

PHOTOMICROGRAPH 5 (AA2153)

Biopsy of cervix of normal primipara 14 hours post-partum. Delivery normal. Note increase in cellularity of stroma and thinning of squamous epithelium, one ragged, collapsed and inactive gland.
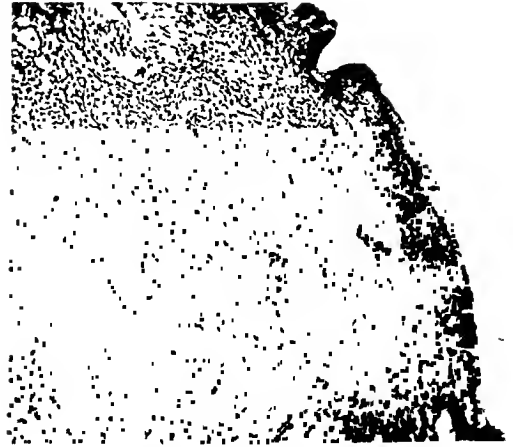
PHOTOMICROGRAPH 6 (AA3512)

Biopsy of cervix of normal primipara 11 days post-partum. Delivery normal. Note very marked increase in cellularity of stroma, perivascular thickening, low inactive endo-cervical epithelium.
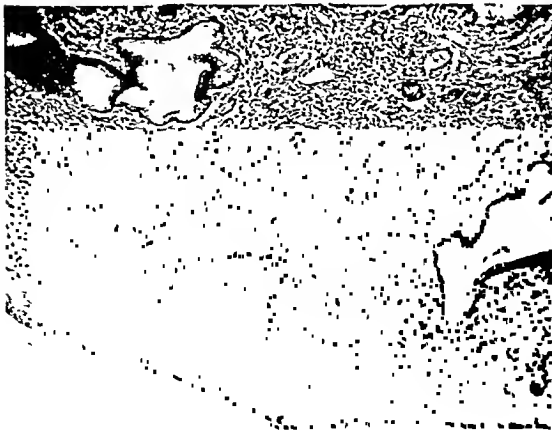
PHOTOMICROGRAPH 7 (AA3446)

Biopsy of cervix of normal primipara 3 months post-partum. Pelvis normal. Complete regeneration of cervix to resting condition, perivascular thickening persists.

M. B. McI.

PHOTOMICROGRAPH 8 (AA1009)

Biopsy of cervix, hyperplastic type primigravida 16 weeks cyesis. Note increase in number and activity of glands compared with normal case.

PHOTOMICROGRAPH 9 (AA920)

Biopsy of cervix hyperplastic type primigravida 25 weeks cyesis. Metaplasia a very marked feature, numerous goblet cells.

PHOTOMICROGRAPH 10 (AA3205)

Biopsy of cervix hyperplastic type primigravida on term. Note numerous glands, some dilated, marked secretory activity and some inflammatory cells.
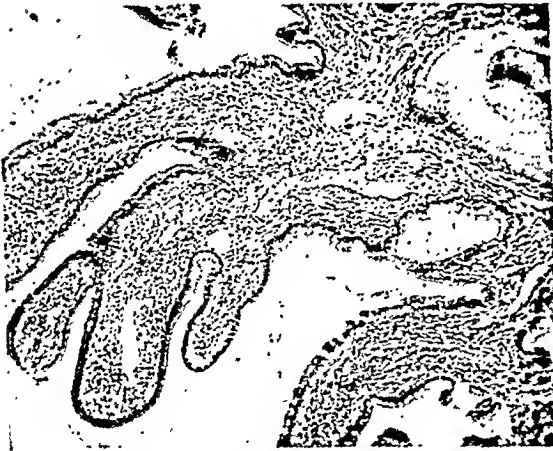
PHOTOMICROGRAPH 11 (AA493)

Biopsy of cervix proliferating type primigravida 14 weeks cyesis. Note marked increase in papillæ and glands. Secretion not a marked feature. Inflammatory cells fairly numerous.

M. B. McI.

PHOTOMICROGRAPH 12 (AA506)

Biopsy of cervix of secreting type primigravida 10 weeks cyesis. Note the widespread metaplasia and numerous goblet cells. There is not much reproduction of glands. Numerous inflammatory cells.

PHOTOMICROGRAPH 13 (AA1008)

Biopsy of cervix of mixed type multipara 10 weeks cyesis. Note proliferation of glands, increased secretory activity and a strip of metaplasia with a few goblet cells. Numerous inflammatory cells.

PHOTOMICROGRAPH 14 (AA1121(i))

Biopsy of cervix normal primigravida 34 weeks cyesis showing widespread metaplasia.

PHOTOMICROGRAPH 15 (AA1121(ii))

Biopsy of cervix normal primigravida 34 weeks cyesis showing marked decidual reaction.

M. B. McI.

TABLE VI (*Continued*).

IIb per cent in 3rd trimester		Complications	Condition of cervix at last prenatal visit	Duration of labour in hours	Nature of delivery	Condition of perineum	Puerperium	Pelvic condition at last postpartum visit	Date of last postpartum visit
				ABNORMAL PRIMIGRAVIDAE					
I.L.	76	—	Healthy	26¼	Normal	Intact	Afebrile	Normal	4½/12
G. McD.	82	—	Healthy	13½	Instrumental	Lacerated	Febrile	Normal	2/12
R.P.	80	—	Healthy	15¾	Instrumental	Lacerated	Febrile	Did not report	
N.N.	75	—	Healthy	15	Instrumental	Lacerated	Febrile	Salpingitis— persisting glycosuria	2/12
E.L.	?	—	Healthy	8½	Normal	Intact	Afebrile	Lacerated cervix—retroversion	5/12
Bc.Go.	?	Patent ductus arteriosus, bronchiectasis	Erosion healing	19¾	Instrumental	Lacerated	Afebrile	Cervical laceration	4/12
P.C.	?	—	Healthy, monilial vaginitis	51¾	Instrumental	Lacerated	Afebrile	Cervical laceration	3/12
M.deM.	78	—	Erosion active	19¼	Normal	Intact	Afebrile	Endo-cervicitis (mild)	4/12
I.S.	77	—	Erosion acute, monilial vaginitis	5	Normal	Lacerated	Febrile	Did not report	5/12
I.P.	90	—	Nabothian follicles ++	15¾	Normal	Intact	Febrile	Normal	5/12
N.T.	75	—	Healthy	13	Normal	Intact	Afebrile	Salpingitis and cervicitis	2½/12
E.E.	81	—	Erosion healing	12¾	Normal	Intact	Febrile	Salpingitis and cervical erosion	2/12
L.B.	82	Pre-eclampsia	Erosion clean	48½	Instrumental	Intact	Afebrile	Normal	2/12
N.B.	89	—	Eroded, mucopus++	7½	Normal	Intact	Febrile	Acute cervical erosion	6½/12
M.L.	98	—	Erosion healing	10	Instrumental	Lacerated	Febrile	Normal	6/12
P.D.	68	—	Healthy	25	Normal	Intact	Febrile	Cervical erosion—retroversion	2½/12
B.H.	75	—	Healthy	17½	Normal	Intact	Afebrile	Retroversion	3/12
B.W.	79	—	Acute erosion	19	Normal	Intact	Afebrile	Normal, cervical erosion—yielded to treatment	4/12
E.H.	85	—	Healthy	19½	Normal	Intact	Afebrile	Normal	3/12
G.A.	75	Avitaminosis	Healthy	20½	Instrumental	Lacerated	Febrile	Subacute salpingitis	3/12

TABLE VI (*Continued*).

	llb per cent in 3rd trimester	Complications	Condition of cervix at last prenatal visit	Duration of labour in hours	Nature of delivery	Condition of perineum	Puerperium	Pelvic condition at last postpartum visit	Date of last post-partum visit
I.R.	77	—	Erosion quiescent	8½	Instrumental	Lacerated	Afebrile	Did not report	
B.J.S.	83	—	Erosion active	3	Normal	Intact	Febrile	Cervical erosion	4½/12
V.I.	85	—	Erosion quiescent	26½	Normal	Intact	Afebrile	Cervical laceration, salpingitis	5/12
J.W.	74	—	Healthy	14½	Instrumental	Intact	Febrile	Subacute cervicitis and salpingitis	3½/12
E.G.	84	—	Erosion	15	Normal	Intact	Afebrile	Normal	3½/12
G.K.	90	—	Healthy	6	Instrumental	Lacerated	Afebrile	Subacute metritis and salpingitis	6½/12
H.M.S.	78	—	Healthy	12	Normal	Intact	Febrile	Cervical laceration	6/52
M.R.	?	—	Polyps present	12½	Normal	Lacerated	Afebrile	Normal	4½/12
B.G.	64	—	Healthy	?	Normal	Intact	Afebrile	No report	
J.McG.	75	—	Polyps present	16	Instrumental	Lacerated	Febrile	Cervical laceration and retroversion	2½/12
E.Au.	82	—	Healthy	15½	Normal	Intact	Afebrile	Normal erosion healed with treatment	4/12
E.An.	88	—	Erosion quiescent	7	Instrumental	Lacerated	Febrile	Report by letter; doctor states pelvis normal	5/12
E.B.	70	Anaemia 2.9 × 10⁶ R.B.C.	Erosion healing	7¾	Normal	Intact	Afebrile	Subacute cervical erosion—subinvolution	6/52
L.A.	74	—	Erosion active, monilial vaginitis	8¾	Instrumental	Lacerated	Febrile	Chronic cervical erosion	5/12
W.M.	82	—	Erosion active	12¾	Instrumental	Intact	Febrile	Subacute salpingitis and cervicitis	3½/12
N.B.	85	—	Erosion active	18	Normal	Intact	Afebrile	Acute cervical erosion	6½/12
J.S.	?	—	Healthy	13	Normal	Lacerated	Afebrile	Normal	3/12
ABNORMAL MULTIPARAE									
M.L.	75	—	Nabothian cyst, monilial vaginitis	5	Normal	Intact	Afebrile	Normal, Bartholin cyst	3/12
R.M.	76	—	Polyps present	7½	Normal	Intact	Afebrile	Normal	3½/12
F.L.	81	—	Endocervicitis	17	Normal	Intact	Afebrile	Cervicitis and salpingitis	3½/12

TABLE VI (*Continued*).

IIb per cent in 3rd trimester	Complications	Condition of cervix at last prenatal visit	Duration of labour in hours	Nature of delivery	Condition of perineum	Puerperium	Pelvic condition at last postpartum visit	Date of last postpartum visit
69	—	Cervix quiescent monilial	10½	Normal	Intact	Afebrile	Mild cervicitis and cervical laceration	5½/12
80	—	Lacerated cervix, mild cervicitis	38½	Instrumental	Intact	Not recorded	Lacerated cervix, retroversion and salpingitis	3/12
?	—	Nabothian follicles mucus + +	14¾	Normal	Intact	Febrile	Did not report	
84	—	Lacerated cervix, monilial vaginitis	5	Normal	Intact	Afebrile	Cervical laceration	6/12
81	—	Cervix lacerated, erosion healing	22	Normal	Intact	Afebrile	Cervix lacerated and acutely eroded	2½/12
64	—	Cervix lacerated, erosion quiescent	12½	Normal	Intact	Afebrile	Subacute metritis and salpingitis, cervix lacerated	4/12
90	—	Cervix lacerated, erosion quiescent	16	Normal	Intact	Afebrile	Subacute cervicitis, metritis and salpingitis, cervical laceration	3/12
?	—	Cervix quiescent	12	Normal	Intact	Afebrile	Subacute salpingitis and cervicitis, cervix lacerated	3/12
85	—	Erosion clean	2½	Normal	Intact	Afebrile	Normal	8/12
?	—	Erosion quiescent	7½	Normal	Intact	Afebrile	Report by letter—discharge and menorrhagia	3/12
?	—	Erosion healing	9	Normal	Intact	Febrile	Chronic cervicitis	3/12
77	—	Polyps present	31¾	Normal	Intact	Febrile	Chronic cervicitis and salpingitis	6/12
?	—	Erosion quiescent	4½	Normal	Intact	Afebrile	Subacute cervicitis, metritis and salpingitis	3½/12
87	—	Erosion quiescent	6¾	Normal	Intact	Afebrile	Acute cervical erosion	2½/12
74	—	Erosion quiescent	20¾	Normal	Intact	Afebrile	Subacute salpingitis, mild cervicitis, anaemia	3/12
95	—	Cervix healthy	2½	Normal	Intact	Afebrile	Normal	4½/12
81	Post-partum II° gc.	Quiescent, lacerated		Normal	Intact	Afebrile	Subacute metritis and salpingitis	7/12
75	—	Lacerated mucopus + +	16¾	Normal	Intact	Afebrile	Cervix acutely eroded and lacerated	3/12

labours lasting over 68 hours. The length of labour for the other 9 patients was under 15 hours except for 1 patient whose labour lasted 42 hours.

In the observation or hyperplastic group 1 patient had an instrumental delivery, her labour lasting 9 hours. All the others delivered · themselves, no labour lasting longer than 24 hours.

In the abnormal primigravidae group 15 patients were delivered by forceps, 1 of them having a labour lasting $51\frac{3}{4}$ hours. All the other labours in this group lasted under 26 hours.

In the abnormal multiparae group only 2 patients had an instrumental delivery. The longest labour in this group was $38\frac{1}{2}$ hours, another was $31\frac{3}{4}$ hours—the remainder were under 20 hours.

Trauma.

The perineum was lacerated 4 times in the normal group, twice in the observation or hyperplastic group, 15 times in the abnormal primigravidae group and not at all in the abnormal multiparae group. Cervical laceration occurred 4 times in the normal group, not at all in the observation group, 5 times in the abnormal primigravidae and once in a patient whose cervix was not torn previously in the abnormal multiparae. It is interesting to note that 3 patients in the normal group, 3 in the abnormal primigravidae and 1 in the abnormal multiparae group suffered cervical lacerations without interference with instruments. It is apparently possible for a patient to force a full-time baby through an incompletely dilated os and tear the cervix herself. It would appear that obstetricians need not take all the blame for cervical lacerations.

Puerperium.

Pyrexia in the puerperium was recorded 8 times in the normal group, 3 times in the observation group, 18 times among the abnormal primigravidae, and 5 times among the abnormal multiparae. Trauma or interference or a prolonged labour may have accounted for 3 cases in the normal group, 1 in the observation group, 12 in the abnormal primigravidae and 1 in the abnormal multiparae.

Pelvic Findings at Final Return Visit.

Patients were seen at 2 to 6 months postpartum. Sometimes only one · visit was made, more often two. When treatment was necessary several visits were paid. The condition at the last visit is the condition reviewed.

Failures to report back were few. There were 2 in the normal group, none in the observation group, 4 among the abnormal primigravidae and 1 among the abnormal multiparae.

Answers to questionnaires were obtained from 4 patients in the normal group, and from 2 in the abnormal primigravidae and 1 in the multiparae groups. In the normal group 1 of these patients complained of premenstrual backache and another had received treatment for retroversion, otherwise both were well.

Two others were well, had no discharge and were nursing satisfactorily. One patient in the abnormal primigravidae group stated that her own doctor had informed her that her pelvic organs were normal. The other 2 had slight discharge but were well and lactating satisfactorily. The abnormal multipara stated that she was not at all well, she had discharge and menorrhagia and had been unable to feed her baby.

The findings in the remaining cases are set out in Table VIII.

Normal pelvic findings were observed in 3 patients in the normal group, in 5 patients in the observation group, in 11 patients among the abnormal primi-

TABLE VIII.
Pelvic Findings at Final Return Visit.

Type of pelvic lesions observed	Normal	Observation	Abnormal primigravidae	Abnormal multiparae
Total cases observed	8	7	32	19
Normal	3	5	11	4
Traumatic lesions	3	—	6	1
Inflammatory lesions	—	2	13	6
Traumatic and inflammatory lesions	2	—	2	8
Failed to return	2	—	4	1

gravidae and in 4 cases among the abnormal multiparae. Clinically healthy cervices at the last antenatal visit were observed in all the normal group, in all the observation group, in 5 cases among the abnormal primigravidae and in 1 case among the abnormal multiparae. The deviations from normal that were observed at the last antenatal visit in these 9 patients were: "clean erosions" (that is no mucopurulent discharge or mucus present) 2 cases; small polypoidal projections of endocervical mucosa from the external os in 2 cases, Nabothian follicles in 2 cases; "healing erosions" (that is, erosions becoming covered with squamous epithelium) in 1 case; and "acute erosion" (that is erosion with mucopurulent discharge and likely to bleed on manipulation) in 1 case. This last patient on her first postnatal visit had an acute erosion which, however, yielded to treatment.

Lesions due to Trauma.

Seven patients had cervical lacerations: of these 3 were normals, 3 abnormal primigravidae and 1 an abnormal multipara whose cervix had not been torn at a previous confinement. One abnormal primigravida had retroversion and 2 had cervical lacerations and retroversion. Of these 7 patients in the abnormal groups 1 had a quiescent cervix and monilial vaginitis at her last antenatal visit; she had a normal delivery and her perineum was

intact; 1 patient who had an instrumental delivery and whose perineum was lacerated had some endocervical mucosal polyps protruding from the os at her last antenatal visit; another patient who had an instrumental delivery and whose perineum was lacerated had a healing erosion at term. The remaining 4 patients had clinically healthy cervices at term, 1 had an instrumental delivery and suffered a perineal laceration; the other 3 had normal confinements, 2 were intact and 1 had a lacerated perineum.

Lesions Due to Inflammation Alone.

No patient in the normal group developed any of these lesions. One patient in the observation group developed salpingitis and 1 a cervical erosion and salpingitis. Both these patients had cervical erosions at their last prenatal visit, both had normal deliveries and intact perinea. Thirteen patients in the abnormal primigravidae group developed inflammatory lesions. They were grouped as follows: salpingitis, 2 cases; salpingitis and metritis, 1 case; cervical erosion, 5 cases; endocervicitis (that is, vaginal surface of the cervix normal, mucopurulent discharge from the os), 1 case; and salpingitis and erosion, 4 cases. All the patients with postnatal erosions entered labour with active erosions, only 1 had an instrumental delivery and perineal laceration, the others all had normal deliveries

and intact perinea. The patient who developed endocervicitis had an active erosion at term, her labour was normal and she suffered no perineal lacerations, as did the patient who developed salpingitis and metritis. All 3 had clinically normal cervices at term. Of the 4 patients who developed salpingitis and a cervical erosion 2 had clinically healthy cervices at their last prenatal visit and 2 had erosions, 1 healing and 1 still active. None of these 4 patients suffered a perineal laceration but 1 patient with a clinically healthy cervix had an instrumental delivery, as did the 1 patient with an active erosion. Six abnormal multiparae developed inflammatory lesions: 2 had cervical erosions at their last prenatal visit and 3 erosion and salpingitis and 1 subacute metritis, salpingitis and erosion. In the erosion group 1 patient had quiescent erosion at term, her confinement was normal and she had no perineal laceration. The other patient had a healing erosion at term, her confinement was normal and her perineum was not lacerated. Of the 3 patients who developed salpingitis and erosion 2 had normal deliveries and no perineal lacerations and 1 an instrumental delivery but no perineal laceration. Their labours lasted respectively, 17, 31¾, and 20¾ hours. One had polypoidal overgrowth of the endocervical mucosa, another endocervicitis, and the third a quiescent erosion at their last prenatal visit. One patient who developed subacute metritis, salpingitis and cervicitis had a quiescent erosion at her last antenatal visit, her labour was normal, lasting 4 hours, and she did not suffer a perineal laceration.

Multiple Lesions—Trauma and Inflammation.

Two patients in the normal group had multiple lesions at their last postnatal visit. One had a lacerated cervix and salpingitis, she had a normal confinement and an intact perineum. The other patient had a retroversion, salpingitis and a cervical erosion. Her delivery had been normal and her perineum intact. Among the abnormal primigravidae 2 patients had multiple lesions at their final postnatal visit. One had a cervical laceration and salpingitis, she entered labour with a clinically quiescent erosion, and a labour lasting 26½ hours and finally delivered herself without a perineal laceration. The other patient developed a retroversion and erosion postpartum. At term she had a healing erosion, her delivery was normal, her perineum intact and her labour lasted 13 hours. Eight patients among the abnormal multiparae developed multiple lesions. Three developed cervical erosion and laceration. All had normal labours and suffered no perineal laceration. At term 1 had a quiescent erosion, the other 2 had cervices already lacerated, 1 had as well a healing erosion and the other a mucopurulent discharge. One patient developed a retroversion and salpingitis superimposed on an already lacerated cervix which was clinically clean at term. She had an instrumental delivery at the end of a labour lasting 38½ hours, her perineum was lacerated. Four patients developed metritis and salpingitis superimposed on an already lacerated cervix which was clinically clean at term. All these patients had normal labours, none of them lasting over 16 hours, and none suffering a perineal laceration.

It is worth noting that of the 33 patients who developed inflammatory lesions 18 had afebrile puerperia.

SIGNS AND SYMPTOMS OF PATIENTS WITH INFLAMMATORY LESIONS SPREADING TO UTERUS AND TUBES.

Thirteen patients had a low-grade salpingitis at their last postnatal visit. The symptoms of which they complained were:

backache, 2; difficulty in lactation, 6; pain in the side or lower abdomen, 5; discharge, 9; bleeding, 3; and dyspareunia, 1. The tubes were palpable in 10 cases, in all 13 there was definite tenderness on bimanual examination of the fornices, 1 patient had a retroposed uterus and 1 had thickening of the utero-sacral ligaments.

Six patients developed metritis after their confinement. The symptoms of which they complained were: bleeding, 1; pain in the lower abdomen, 5; difficulty in lactation, 4; discharge, 5; weakness, 1; and headaches, 1. The uterus was tender in all 6 cases, subinvoluted once. One patient developed a postpartum monilial vaginitis. She had not suffered from this during her pregnancy.

The difficulty experienced by these patients with lactation was striking and it was found that when the mothers stopped nursing there was a rapid improvement in their pelvic condition.

Assessment of Results.

The first fact that is obvious from a study of these results is that only 2 patients in the normal group developed inflammatory lesions and both these patients had suffered traumatic lesions as well. In the observation or hyperplastic group 2 patients who entered labour with active erosions developed inflammatory lesions though they suffered no trauma. In the abnormal primigravidae nearly half the patients (15) developed inflammatory lesions though only 2 of these patients had suffered traumatic lesions as well. In the abnormal multiparous group about two-thirds (14) developed inflammatory lesions and 8 of these patients had suffered trauma as well.

Of the 23 patients who had no pelvic abnormality at their final visit all had clinically healthy cervices or minor deviations from normal at the last prenatal visit.

While it is admitted that the number of cases is small and figures are often misleading it seems reasonable to conclude that:

1. These cervical lesions constitute a definite danger to the mother and increase her chances of developing a low-grade pelvic infection after confinement.

2. Among abnormal primigravidae the added factor of cervical trauma does not seem to play a very big part.

3. Among multiparae on the other hand the presence of pre-existing trauma and trauma developing at the labour under consideration seem to aggravate the tendency to develop inflammatory lesions and to encourage spread to the uterus and adnexae.

4. An afebrile puerperium is no guarantee that the patient will escape further trouble.

The clinical applications of these findings are:

1. Every patient should have her cervix inspected at each antenatal visit just as faithfully as her blood-pressure is taken. Symptoms may be unnoticed by the patient and lesions may develop during the course of the pregnancy.

2. Every endeavour to improve the condition of the cervix should be made during pregnancy. The treatment found most satisfactory in this clinic was application of penicillin-sulphanilamide powder and vitamin-B therapy.

3. Every patient should be followed up for at least 8 weeks post-partum as spreading lesions may not appear before that period.

4. If a woman with a cervical erosion is seen before marriage everything possible should be done to cure the condition in view of the risk of developing a low-grade pelvic inflammation after a pregnancy.

5. Lactation is often very poor among these patients in the postnatal period. It is amazing how rapidly the pelvic lesions

retrogress and the patients improve in general health when the baby is weaned.

Although no light has been thrown on the cause of these lesions, a study of biopsies throughout pregnancy, the puerperium and postpartum for intervals up to 6 months has revealed something of their progress and nature. It would appear necessary to combine hormonal assays, animal bacteriological experiments and clinical studies to elucidate fully their role in pelvic disease following labour.

SUMMARY.

1. A review of the history and our present knowledge of puerperal infection is given. To date little study of cervical pathology has been undertaken to elucidate the problem of morbidity.

2. Seventy-seven cases were studied throughout pregnancy, in the puerperium and postpartum—of these 12 were normal, 7 cases referred as normal but classified as "For observation", 37 were primigravidae and 21 multiparae suffering from leucorrhoea.

4. pH findings, cells seen in smears from cervix, vagina and urethra, and cultures taken from these areas are described.

5. Biopsies were taken at intervals throughout pregnancy, the puerperium and postpartum. From a study of these, normal changes in the cervix were recognized and are described and 4 deviations from normal are classified and described. They are hyperplastic, proliferative, secretory and mixed types.

6. The antenatal treatment given is reviewed. The best results were obtained with penicillin-sulphanilamide powder applied to the cervix, combined with administration of vitamin B.

7. The condition of the patients at the onset of labour and the complications occurring are described.

8. The nature of the labour and puerperium and any interference and trauma that may have occurred are reported.

9. The condition of the patient and the presence of traumatic or inflammatory pelvic lesions, or of both combined, at the final follow-up visit are described.

10. Conclusions with regard to treatment and prevention are given.

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The Range of Blood-Pressure among Women who had a Normal Pregnancy and Confinement

BY

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THE significance which could be attached to high blood-pressures during pregnancy was carefully considered during the planning of the investigation made by The People's League of Health into " The Nutrition of Expectant and Nursing Mothers in Relation· to Maternal and Infant Mortality and Morbidity."[*] The original intention had been to classify as toxaemia (*a*) cases which exhibited hypertension—a systolic blood-pressure of or above 140 mm. Hg, or a diastolic pressure of or above 90 mm. Hg, with or without albuminuria, and (*b*) cases in which there was no hypertension and in which the diagnosis was based upon albuminuria. This was modified since " within recent years, and increasingly since the date at which this investigation was planned and the standard as given above laid down, it has come to be recognized that a diagnosis of toxaemia cannot be based upon hypertension by itself, as this frequently connotes not a true or specific pregnancy toxaemia but an essential hypertension." One of the chief difficulties in attempting to fix a range of blood-pressures that could be regarded as normal for pregnant women was the paucity of data. The number of blood-pressures taken during the investigation was, however, sufficiently large to make an inde-

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pendent study by age and parity of the trend and range of blood-pressures during pregnancy.

THE DATA.

The data are based on the blood-pressures of the women who took part in the nutrition inquiry. These women were booked cases at 10 London maternity hospitals, and had enrolled at the antenatal clinic before the 24th week of pregnancy. In addition to the women rejected from the original inquiry because of some disease or abnormality a further selection was made by excluding all women who did not have a normal confinement or who had toxaemia during pregnancy. All cases of hypertension not accompanied by other symptoms were included since the object of this paper is to examine the range of blood-pressures among women who had an uneventful pregnancy and confinement. No distinction has been made between the 2 groups of women in the original inquiry, and the women who received supplements and the controls have been combined. The numbers which were available for analysis were:

	Primiparae	Multiparae
Number of women	2,538	1,788
Number of blood-pressure observations	20,239	13,678
Average per woman	7.65	7.97

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TABLE I.
Systolic Blood-pressure.

No. of weeks before delivery	Primiparae			Multiparae		
	No. of observations	Mean and S.E.	S.D.	No. of observations	Mean and S.E.	S.D.
Ages under 25						
24 and over	337	120.0 ± 0.65	11.8	81	117.9 ± 1.28	11.5
20–24	465	119.4 ± 0.52	11.2	147	116.7 ± 0.94	11.4
16–20	735	117.5 ± 0.41	11.3	240	117.3 ± 0.73	11.3
12–16	990	117.8 ± 0.34	10.8	309	116.1 ± 0.57	10.0
11–12	283	117.9 ± 0.67	11.2	83	116.5 ± 1.1	10.1
10–11	326	·117.0 ± 0.62	11.1	98	116.9 ± 1.18	11.7
9–10	309	117.7 ± 0.57	10.8	86	117.9 ± 0.97	9.0
8–9	369	119.2 ± 0.57	10.9	110	115.4 ± 1.07	10.9
7–8	408	118.9 ± 0.53	10.7	113	116.7 ± 1.09	11.6
6–7	427	119.2 ± 0.52	10.8	121	118.4 ± 1.03	11.4
5–6	510	118.7 ± 0.51	11.6	110	116.4 ± 1.06	11.1
4–5	511	119.0 ± 0.46	10.4	149	117.9 ± 0.94	11.5
3–4	593	119.4 ± 0.44	10.7	166	117.7 ± 0.81	10.4
2–3	641	120.9 ± 0.46	11.7	166	118.4 ± 0.98	12.6
1–2	711	120.9 ± 0.41	10.9	188	119.7 ± 0.75	10.3
0–1	574	121.8 ± 0.49	11.7	157	118.9 ± 0.92	11.5
All periods	8189	119.2 ± 0.12	11.2	2324	117.4 ± 0.23	11.1
Ages 25–29						
24 and over	442	119.6 ± 0.58	12.2	244	118.4 ± 0.72	11.2
20–24	601	119.9 ± 0.46	11.3	311	116.8 ± 0.59	10.5
16–20	773	119.5 ± 0.42	11.6	501	117.6 ± 0.48	10.7
12–16	1004	119.7 ± 0.35	11.1	617	117.3 ± 0.46	11.4
11–12	272	119.5 ± 0.65	10.6	182	118.0 ± 0.80	10.7
10–11	310	120.2 ± 0.66	11.6	187	117.1 ± 0.79	10.9
9–10	338	119.6 ± 0.61	11.3	198	117.5 ± 0.74	10.4
8–9	346	120.0 ± 0.57	10.5	220	117.6 ± 0.77	11.4
7–8	406	119.9 ± 0.52	10.5	218	118.2 ± 0.75	11.0
6–7	418	121.1 ± 0.56	11.5	239	118.2 ± 0.72	11.1
5–6	512	120.3 ± 0.53	11.9	274	118.1 ± 0.68	11.3
4–5	530	121.1 ± 0.49	11.2	321	118.9 ± 0.64	11.5
3–4	638	121.1 ± 0.46	11.5	336	119.4 ± 0.58	10.6
2–3	653	122.1 ± 0.47	11.9	359	118.8 ± 0.56	10.6
1–2	711	121.3 ± 0.43	11.6	401	118.8 ± 0.60	11.9
0–1	567	123.3 ± 0.50	11.9	354	120.7 ± 0.63	11.8
All periods	8521	120.6 ± 0.12	11.5	4962	118.2 ± 0.16	11.2
Ages 30 and over						
24 and over	197	121.4 ± 0.78	11.0	358	119.2 ± 0.61	11.5
20–24	243	120.8 ± 0.75	11.8	462	118.2 ± 0.49	10.6
16–20	319	120.6 ± 0.71	12.7	676	118.9 ± 0.46	12.1
12–16	399	120.0 ± 0.61	12.2	798	118.6 ± 0.40	11.2
11–12	113	117.6 ± 1.12	11.9	190	118.4 ± 0.83	11.4
10–11	139	121.0 ± 0.87	10.2	268	117.3 ± 0.69	11.3
9–10	112	120.5 ± 1.23	13.0	249	119.3 ± 0.70	11.1
8–9	164	120.0 ± 0.92	11.8	273	120.1 ± 0.69	11.5
7–8	162	121.7 ± 0.90	11.5	271	118.9 ± 0.67	11.0
6–7	186	120.5 ± 0.84	11.4	337	119.1 ± 0.65	11.8
5–6	206	120 7 ± 0.81	11.6	327	119.2 ± 0.62	11.3
4–5	221	121.2 ± 0.81	12.1	408	120.0 ± 0.59	12.0
3–4	259	121.8 ± 0.76	12.2	419	119.7 ± 0.59	12.0
2–3	275	122.5 ± 0.68	11.3	479	120.4 ± 0.57	12.4
1–2	296	123.3 ± 0.69	11.9	457	121.3 ± 0.56	12.0
0–1	238	123.7 ± 0.76	11.7	420	121.7 ± 0.57	11.7
All periods	3529	120.1 ± 0.20	12.0	6392	119.4 ± 0.15	11.7

SYSTOLIC PRESSURE.

The mean systolic blood-pressure in mm. Hg by age, parity and by length of period before delivery is shown in Table I. This table shows that a gradual but irregular rise in systolic blood-pressure, for both the primiparae and multiparae in each of the 3 age groups, occurred during the last weeks of pregnancy. In each age group the systolic blood-pressure of the multiparae was consistently below that of the primiparae throughout pregnancy. A small progression with age was apparent in the blood-pressures of the multiparae but not for the primiparae and it appears that parity is more important than age in determining the level of the systolic blood-pressure. A comparison of the percentage distribution of the systolic readings during the last 4 weeks of pregnancy is made in Table II.

The 3 age groups were combined, since age had only a slight effect on systolic pressure. Just over one third of the readings of both the primiparae and the multiparae fell within the group 115–124 mm. Hg; 36.2 per cent of the primiparae and 30.6 per cent of the multiparae had systolic pressures of 125 mm. Hg or more.

TABLE II.

Percentage Distribution of Systolic Blood-pressures During 0–4 Weeks Before Delivery. All Ages Combined.

mm. Hg	Primiparae		Multiparae	
	No. of readings	Per-centage	No. of readings	Per-centage
Under 95	41	0.67	47	1.20
95–	376	6.11	282	7.23
105–	1234	20.04	956	24.50
115–	2276	36.97	1422	36.44
125–	1548	25.15	847	21.71
135–	554	9.00	284	7.28
145–	92	1.49	46	1.18
155 and over	35	0.57	18	0.46
Total	6156	100.00	3902	100.00

There was little difference in the proportion of women suffering from hypertension in the 2 groups; 2.06 of the primiparae and 1.64 of the multiparae had systolic pressure of 145 and more.

DIASTOLIC PRESSURE.

The diastolic blood-pressure in mm. Hg by parity, age and length of period before confinement are shown in Table III. The diastolic pressure displayed a trend similar to that of the systolic pressure. An increase in diastolic blood-pressure occurred during pregnancy in each age group of the primiparae and multiparae.

TABLE IV.

Percentage Distribution of Diastolic Blood-pressure During 0–4 Weeks Before Delivery. All Ages Combined.

mm. Hg	Primiparae		Multiparae	
	No. of readings	Per-centage	No. of readings	Per-centage
Under 45	9	0.15	7	0.18
45–	76	1.23	65	1.67
55–	848	13.78	561	14.37
65–	2358	38.30	1558	39.93
75–	2086	33.89	1333	34.16
85–	639	10.38	323	8.28
95–	122	1.98	44	1.13
105 and over	18	0.29	11	0.28
Total	6156	100.00	3902	100.00

The primiparae had, for each age group, a larger average diastolic pressure than the multiparae. The percentage distribution of the diastolic blood-pressures during the last 4 weeks of pregnancy for all ages combined is shown in Table IV.

Seventy-two per cent of the primiparae and 74 per cent of the multiparae had a diastolic blood-pressure between 65–84; 2.27 per cent of the primiparae and 1.41 per cent of the multiparae had readings of 95 mm. or more.

TABLE III.

Diastolic Blood-pressure.

No. of weeks before delivery	Primiparae			Multiparae		
	No. of observations	Mean and S.E.	S.D.	No. of observations	Mean and S.E.	S.D.
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24 and over	337	68.3 ± 0.57	10.4	81	69.4 ± 1.22	11.0
20–24	465	68.0 ± 0.42	9.1	147	68.0 ± 0.90	10.9
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12–16	990	68.2 ± 0.29	9.1	309	68.3 ± 0.47	8.3
11–12	283	68.4 ± 0.54	9.0	83	67.1 ± 0.94	8.6
10–11	326	68.4 ± 0.50	9.0	98	68.4 ± 0.90	8.9
9–10	309	69.9 ± 0.58	10.3	86	68.0 ± 0.85	7.9
8–9	369	69.6 ± 0.43	8.3	110	69.1 ± 0.85	8.9
7–8	408	70.2 ± 0.45	9.1	113	68.9 ± 0.91	9.7
6–7	427	70.4 ± 0.45	9.2	121	70.3 ± 0.83	9.1
5–6	510	71.0 ± 0.44	10.0	110	69.6 ± 0.93	9.7
4–5	511	72.5 ± 0.42	9.5	149	71.6 ± 0.74	9.0
3–4	593	72.2 ± 0.42	10.2	166	71.5 ± 0.75	9.7
2–3	641	73.6 ± 0.39	9.8	166	72.6 ± 0.69	8.9
1–2	711	74.2 ± 0.34	9.2	188	72.6 ± 0.65	8.9
0–1	574	75.3 ± 0.43	10.4	157	74.4 ± 0.76	9.5
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0–1	567	76.1 ± 0.40	9.6	354	75.1 ± 0.51	9.6
All periods	8521	72.0 ± 0.11	9.8	4962	70.9 ± 0.14	9.5
Ages over 30						
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20–24	243	71.8 ± 0.62	9.7	462	70.5 ± 0.44	9.5
16–20	319	71.0 ± 0.55	9.8	676	70.5 ± 0.37	9.6
12–16	399	71.1 ± 0.48	9.7	798	70.2 ± 0.32	9.1
11–12	113	71.2 ± 0.94	10.0	190	70.8 ± 0.64	8.9
10–11	139	72.1 ± 0.76	8.9	268	69.9 ± 0.52	8.5
9–10	112	72.6 ± 0.88	9.3	249	71.0 ± 0.57	9.1
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4–5	221	73.7 ± 0.72	10.8	408	72.7 ± 0.50	10.1
3–4	259	74.4 ± 0.60	9.7	419	73.2 ± 0.44	8.9
2–3	275	75.4 ± 0.62	10.3	479	73.8 ± 0.45	9.9
1–2	296	76.1 ± 0.60	10.2	457	74.9 ± 0.44	9.4
0–1	238	76.2 ± 0.64	9.8	420	75.2 ± 0.49	10.1
All periods	3529	73.2 ± 0.17	10.0	6392	72.0 ± 0.12	9.5

SUMMARY.

The analysis of 33,917 systolic and diastolic blood-pressures of women who had an uneventful pregnancy and a normal confinement showed:

1. The primiparae had a higher average blood-pressure at each age and at each period during pregnancy than the multiparae.

2. A rise in both systolic and diastolic blood-pressure occurred during the last 2 months of pregnancy among the primiparae and multiparae in each age group.

3. The rise in blood-pressure with increasing age is small.

4. Diastolic pressure is more sensitive than systolic pressure during pregnancy; the average increase was twice as large for diastolic pressure as for systolic pressure.

5. If the normal range of blood-pressure is defined by the mean ± twice the standard deviation then systolic pressures above 145 and diastolic pressures above 95 should be considered abnormal.

The Value of the Guterman Test in Threatened Abortion

BY

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THE use of progesterone in cases of threatened abortion is a well-established practice. Its administration was originally based on the work of Knaus (1929) who demonstrated that in the presence of an active corpus luteum of normal cycle or of pregnancy, the spontaneous contractions of the uterus, evident during the follicular phase of the menstrual cycle, cease. Consequently progesterone was considered a "uterine sedative."

But not all clinicians are convinced of the efficacy of progesterone in threatened abortion, and some assert that its administration may even favour progress of the abortion. There is experimental evidence to support these views. Schultze (1931) found that there is a pattern of uterine contractions characteristic of the follicular phase and another pattern characteristic of the luteal phase. The latter is marked by an increase in the amplitude and a decrease in the frequency of the contractions. These findings, which were subsequently confirmed by Moir (1936) and by Henry and Browne (1943), are generally accepted to-day, and would explain the adverse results which are sometimes seen when progesterone is administered in cases of threatened abortion. In cases where the administration of progesterone has apparently relieved the threat of abortion, its action may have been by virtue of its ability to maintain the decidua and improve the foetal-maternal vascular connexions.

From the standpoint of therapy, therefore, it would be desirable to divide cases of threatened abortion into two groups—(1) those accompanied by evidence of progesterone deficiency, and (2) those not so accompanied. Progesterone therapy might then be limited to cases coming within the first group.

The distinction between the two groups can be made by means of urinary pregnanediol excretion tests.

THE THEORETICAL BASIS OF URINARY PREGNANEDIOL EXCRETION TESTS

The role of progesterone in the physiology of menstruation and reproduction was established by Corner and Allen in 1928. The isolation of pregnanediol from the urine by Marrian (1929) was followed by work establishing this substance as the urinary excretion product of progesterone. Briefly, this point was proved by showing that: (a) Pregnanediol excretion coincides with the period of corpus luteum activity in the ovular menstrual cycle (Venning and Browne, 1937); (b) In normal pregnancy, when the corpus luteum persists, the execretion of pregnanediol in the urine also persists (Venning and Browne, 1940); (c) Administration of progesterone is followed by the appearance of pregnanediol in the urine (Venning, Henry and Browne, 1937).

In 1937 Venning described his gravimet-

ric method of biochemical assay of urinary pregnanediol. Since then many studies have been made of pregnanediol excretion in the urine of pregnant women and non-pregnant women; and the increased pregnanediol excretion in the urine of pregnant women was employed for the diagnosis of pregnancy by several workers, including Hain and Robertson (1939) in this country.

All these workers employed the Venning method of extraction of pregnanediol in the form of sodium pregnanediol glycuronidate, a method which is laborious and time-consuming, requiring a litre of a 24-hour specimen of urine and taking 2 or 3 days to complete.

In 1944 Guterman described the test which bears his name, and which he originally applied to the diagnosis of of pregnancy. The basis of the test is the application of the colour-complex which develops when pregnanediol is dissolved in concentrated sulphuric acid —this colour reaction was originally described by Kober (1931)—to a rapid method of pregnanediol extraction described by Astwood and Jones (1941).

The Procedure of the Guterman Test.

The Guterman test (Guterman, 1944, 1945) consists of 5 steps:

(1) The hydrolysis and extraction with toluene of pregnanediol from a 100 ml. specimen of urine. (2) The precipitation of impurities with 2 per cent sodium hydroxide in absolute methanol. (3) The precipitation of pregnanediol in acetone and N/10 sodium hydroxide. (4) The isolation of pregnanediol. (5) The development of a colour-complex when 10 ml. concentrated sulphuric acid is added to the extracted pregnanediol.

A deep yellow to brown colour is "positive", a yellow or colourless solution is "negative." According to Guterman (1946) more than 0.4 mg. pregnanediol in the 100 ml. urine gives a positive test.

The test can be carried out in less than 3 hours, is inexpensive, requires accuracy but no great technical skill, and utilizes a comparatively small amount of urine.

The Application of Pregnanediol Assays to Threatened Abortion.

There is a pattern of urinary pregnanediol excretion in pregnancy despite individual quantitative variations. Up to about the 9th week after the last menstrual period the excretion equals or, more commonly, slightly exceeds that of the height of the luteal-phase of the ovular menstrual cycle. After about the 9th week, there is a sharp rise in pregnanediol output which reaches a maximum 2 or 3 weeks before labour, when a decline sets in. Pregnanediol finally disappears from the urine within 5 days of delivery. The sharp rise referred to may coincide with the transfer of the site of progesterone production from the corpus luteum of pregnancy to the placenta, which transfer is now generally held to occur at the 8th/10th week of pregnancy. The decline prior to labour can be ascribed to the gradual degeneration of the placenta at that time.

Clinically, abortion is common at this time of transfer of progesterone production from corpus luteum to placenta, and Browne, Henry and Venning (1939) pointed out that failure to maintain progesterone production during the transfer may be the cause of abortion at this period of pregnancy. Investigating pregnanediol excretion in threatened abortion, they found that persistence of pregnanediol excretion in the urine at a reasonable level was associated with continuation of pregnancy, but that a fall in, or the absence of, excretion was usually followed by abortion.

These observations were confirmed by

Cope (1940) and Hain (1942). But all these workers emphasized the prognostic value of such assays rather than their value as a guide to rational treatment of threatened abortion. To some extent this was inevitable because the method of Venning, which they employed, took 3 or 4 days to complete, and by that time the outcome of the case was usually settled, or at any rate the optimum time for progesterone therapy, if indicated, had passed.

In 1946 Guterman reported on his use of his test in 73 cases of threatened abortion, but he, too, concentrated on the prognostic value of the test. He reported that in 68 out of the 73 cases he had succeeded in giving a correct forecast of the outcome of pregnancy. Where the test was negative, abortion ensued with 1 exception, and where the test was positive, the pregnancy continued with 4 exceptions.

Guterman ascribed these last 4 failures to: (1) Cases where factors other than progesterone deficiency were found responsible for abortion, e.g., fibroids, retroversion. In these cases, abortion occurred despite a positive test. (2) Cases where he had performed only one test. He pointed out that if the pregnanediol output is originally high, as it may be normally after the 12th week, then even after a fall the excretion figure may still be above the maximum level for a negative test. He therefore advised that where the test is positive, but not strongly so, it should be repeated on the following days to see whether excretion is decreasing; which latter would indicate hormonal failure and suggest inevitability of the abortion ensuing.

He further concluded from the last point that it was desirable to apply a method of quantitative assay to his test. This has been done in the present investigation.

The Present Investigation.

The present investigation was undertaken in a preliminary series of 57 cases diagnosed clinically as threatened abortion. Fifty-five of the cases were followed up. It subsequently transpired that an error in diagnosis was made in 14 cases, in most of which the Guterman test, together with either a simultaneous Aschheim-Zondek test or the clinical course of the case, established the correct diagnosis.

The objects of the investigation were:

(1) To evaluate the Guterman test as a practical method of dividing cases of threatened abortion into the 2 groups mentioned previously—those with and those without evidence of progesterone deficiency.

(2) To take advantage of the quickness of the test in order to employ it as a guide, not merely to prognosis, but to treatment of the cases.

The technique of the test as employed in the present investigation was as described by Guterman (1944, 1945, 1946) together with minor modifications kindly described by Guterman in a personal communication. The details of the technique are given in Appendix A.

A quantitative method of assay has been applied to the test by using a Spekker photo-electric absorptiometer. A colour-strength calibration curve is obtained by using measured amounts of pure pregnanediol dissolved in concentrated sulphuric acid, and the strength of any test solution is read off from the calibration curve. The details of this method are given in Appendix B.

In 39 out of the 55 cases an Aschheim-Zondek test was carried out simultaneously, and valuable information was often obtained by comparing the results of the two tests in the same case.

Interpretation of the Test Results.

A negative result, or with consecutive daily tests, a decreasingly positive result, is taken to indicate one of two possibilities.

(1) Firstly, the pregnancy, although still alive, is endangered by progesterone deficiency. This type of case is eminently suitable for progesterone therapy, and it has been found that 10 mg. of progesterone daily is a sufficient dosage to restore the urinary pregnanediol level to a normal figure in most cases.

In the absence of progesterone therapy in these cases there still remains a possibility of spontaneous cure. For instance, Jones and Weil (1938) recorded an interesting case where, after the removal of the corpus luteum of pregnancy on the 58th day after the last menstrual period without interruption of gestation, pregnanediol was absent from the urine for 12 days, after which it reappeared in increasing amounts.

It must also be borne in mind that in some cases of threatened abortion there may be more than one aetiological factor, and that progesterone deficiency may be accompanied by some other fault such as for instance, retroversion. This emphasizes the need for careful clinical examination in all cases for, if a successful outcome is to be obtained, treatment must be directed against all known factors concerned in the abortion.

(2) Alternatively, the negative test may be evidence that the pregnancy is already dead or the condition already irreversible and beyond response to therapy. This emphasizes the point that what is clinically termed " threatened abortion " covers not only the condition of true threatened abortion, but also the condition of threatened expulsion of a missed abortion. It is in the latter category of case that the simultaneous performance of an Aschheim-Zondek test has proved valuable, in that a weak positive or negative Aschheim-

Zondek test has demonstrated the true nature of the case.

A positive result, or, in consecutive daily tests, a maintained positive result, indicates that the pregnancy is not threatened by progesterone deficiency. A diligent search should therefore be made for other causes for abortion, general or local.

Possible Causes of False Test Results.

The result of the test may be vitiated under certain circumstances:

(1) *Diuresis.* It was found, by performing the test in 5 cases of normal pregnancy on separately collected portions of the 24-hour specimen of urine, that the concentration of pregnanediol was highest in the first morning specimen, and that in some afternoon specimens the concentration was barely sufficient to give a positive test. For example, in a case of normal pregnancy at 20 weeks, the following results were obtained:

100 ml. first morning specimen of urine —Strong positive (4.20 mg.).

100 ml. late afternoon specimen—Weak positive (0.48 mg.).

100 ml. whole 24-hour specimen— Positive (0.88 mg.).

From this it is apparent that for reliability the first morning specimen of urine must be employed for the test.

(2) *Kidney disease.* Cope (1940) pointed out that the excretion of pregnanediol would be affected by kidney disease and in a case of normal pregnancy with chronic nephritis he found a low pregnanediol excretion. This was confirmed in a similar case which was seen and tested during the time of the present investigation. The urinary pregnanediol was 0.50 mg. in 100 ml. first morning specimen of urine at 16 weeks after the last menstrual period.

(3) *Previous administration of Progesterone.* The administration of progesterone is followed by the appearance of preg-

GROUP I. *Threatened Abortion. Positive Guterman Tests* (28).

Test No.	Date	Guterman test	Aschheim-Zondek Reaction	Progesterone given after test	Aborted	Remarks
39	28/10/46	Positive	Toxic	No	No	Full-time delivery.
50	12/11/46	Positive	Positive	No	No	
54	18/11/46	Positive	Positive	No	No	
57	29/11/46	Positive	Positive	No	No	Retroversion corrected
59	4/12/46	Positive (0.62 mg.)	—			
	5/12/46	Positive (0.86 mg.)	—	No	No	
	6/12/46	Positive (0.86 mg.)	—			
61	12/12/46	Positive (0.52 mg.)	—	No	No	
	13/12/46	Positive (0.62 mg.)	—			
68	18/ 1/47	Positive	—	No	No	Three previous abortions at 10 weeks.
71	18/ 1/47	Positive	—	No	No	After nephrectomy.
73	6/ 2/47	Positive	—	No	No	One previous abortion.
75	10/ 2/47	Positive	—	No	No	
77	13/ 2/47	Positive	—	No	No	
80	17/ 2/47	Positive (0.60 mg.)	—			Retroversion corrected.
	18/ 2/47	Positive (0.68 mg.)	—	No	No	
90	7/ 3/47	Positive	Toxic positive	No	No	
91	10/ 3/47	Positive	Positive	No	No	
106	26/ 3/47	Positive	Positive in dilution	No	No	Twins.
107	28/ 3/47	Positive	—	No	No	
108	1/ 4/47	Positive	Positive in dilution	No	No	
27	25/10/46	Positive	Positive	No	Yes	Retroversion.
52	14/11/46	Positive	Positive	No	Yes	Fibroids.
67	12/ 1/47	Positive	—	No	Yes	Bicornuate uterus, 3 previous abortions.
72	22/ 1/47	Positive	Positive	No	Yes	No cause found.
102	24/ 3/47	Positive	—	No	Yes	Retroversion corrected 3 weeks before test. Hysterosalpingography normal. Three previous abortions.
8	1/10/46	Positive	Positive	Yes	Yes	
28	29/10/46	Positive	Positive	Yes	Yes	
62	13/12/46	Positive	Positive	Yes	Yes	
76	12/ 2/47	Positive	—	Yes	No	Four previous abortions.
103	24/ 3/47	Positive	Positive	Yes	No	
112	2/ 4/47	Positive	Positive	Yes	No	

GROUP II. *Threatened Abortion—Negative Guterman Tests* (11).

Test No.	Date	Guterman test	Aschheim-Zondek Reaction	Progesterone given after test	Aborted	Remarks
11	8/ 8/46	Negative	Positive	No	Yes	
12	16/ 8/46	Negative	Positive	No	Yes	
14	8/10/46	Negative	Positive	No	No	Full-time delivery.
83	27/ 2/47	Negative	Positive	No	Yes	
92	10/ 3/47	Negative	Positive	No	Yes	
113	8/ 4/47	Negative	—	No	Yes	
7	30/ 9/46	Negative	Positive	Yes	No	
25	24/10/46	Negative	Positive	Yes	No	
48	15/11/46	Negative	Positive	Yes	No	
110	1/ 4/47	Negative	Positive	Yes	No	
79	18/ 2/47	Negative	Positive	Yes	Yes	

nanediol in the urine (Venning, Henry and Browne, 1937). The result of the test is therefore vitiated if progesterone has been administered prior to the collection of urine for the test.

Results of the Present Investigation.

The Guterman test was carried out in 57 cases diagnosed clinically as threatened abortion, and 55 of these were followed up. The follow-up extended primarily for a limited period of 6 weeks from the day of the test, because the result of the test was only

complete abortion—Negative tests (11); (5) Not pregnant—Positive tests (2); (6) Not pregnant—Negative tests (1).

Comment (Group I). In this group of positive tests, of the 22 cases where progesterone was not given, 17 did not abort (in 2 of whom another cause for abortion was found and treated), and 5 did abort (in 4 of whom a possible cause for abortion was later found).

Of the 6 cases where progesterone was given after the test, 3 did not abort and 3 did abort. In the latter, no other cause for

GROUP III. *Threatened Abortion— Vitiated Guterman Tests* (2).

Test No.	Date	Guterman test	Aschheim-Zondek Reaction	Progesterone given after test	Aborted
47	15/11/46	Positive	—	No	Yes
60	8/12/46	Positive	Positive	Yes	No

GROUP IV. *Missed and Complete Abortion—Negative Guterman Tests* (11).

Test No.	Date	Guterman test	Aschheim-Zondek Reaction	Progesterone given after test	Diagnosis
10	3/10/46	Negative	Negative	No	Missed abortion
18	10/10/46	Negative	Weak positive	Yes	
	16/10/46	—	Negative	—	Missed abortion
33	4/11/46	Negative	Positive	No	Missed abortion
65	15/12/46	Negative	—	Yes	Missed abortion
74	8/ 2/47	Negative	Negative	No	Complete abortion
81	25/ 2/47	Negative	Negative	No	Complete abortion
87	6/ 3/47	Negative	Toxic	No	Missed abortion
94	12/ 3/47	Negative	Negative	Yes	Missed abortion
98	17/ 3/47	Negative	Weak positive	Yes	Complete abortion
111	2/ 4/47	Negative	Negative	No	Missed abortion
118	16/ 4/47	Negative	Negative	No	Complete abortion

significant of the urinary pregnanediol level at the time of the test. Fifty-two of the patients were or had been pregnant, and 3 had conditions unassociated with pregnancy.

The series falls naturally into six groups —(1) Threatened abortion—Positive tests (28); (2) Threatened abortion—Negative tests (11); (3) Threatened abortion—Vitiated tests (2); (4) Missed abortion and

abortion was found and it is possible that the administration of progesterone may have accelerated the abortion. However, it should be noted that in 15 of the 17 cases where progesterone was not given and abortion did not follow, as well as in the 3 cases where progesterone was given and abortion did not follow, the cause of the threat to the pregnancy was not discovered.

Comment (Group II). In this group of negative tests, of the 5 cases where progesterone was given, 4 did not abort and 1 did abort; whereas of the 6 cases where progesterone was not given, 1 did not abort and 5 did.

These figures suggest that where there is evidence of progesterone deficiency in threatened abortion, the prompt administration of progesterone may avert abortion unless the condition is already irreversible, or the progesterone deficiency is not the sole factor favouring abortion.

If progesterone is not given, spontaneous cure may follow, but more commonly abortion ensues.

Comment (Group III.) The test is vitiated by prior administration of progesterone, but it is probably safer to continue giving progesterone in these cases than to discontinue it.

Comment (Group IV). The correct diagnosis in these was established subsequent to the Guterman test by either the result of the Aschheim-Zondek reaction or the clinical course of the case, 'or both'. In some cases progesterone was given on the strength of the Guterman Test result, before the correct diagnosis was established.

It may be difficult in early pregnancy to differentiate between threatened abortion and complete abortion which has occurred before the patient was first seen.

GROUP V.
Not Pregnant. Positive Guterman Tests (2)

Case No.	Date	Guterman test	Aschheim-Zondek reaction
15	9/10/46	Positive	Negative
	16/10/46	Positive	Negative
	1/11/46	Negative	—
22	20/10/46	Positive	Negative

Comment (Group V). These cases both presented a period of 2 months' amenor-

rhoea followed by slight bleeding at a time corresponding to that of a menstrual period. In both, the uterus was slightly enlarged and softened and 'a cyst was palpable in 1 ovary. In 1, there were also signs of breast activity with secretion. These were presumably cases of cyst of the corpus luteum. The cysts retrogressed spontaneously over a period of 2 to 3 months and normal menstruation was resumed.

GROUP VI.
Not Pregnant. Negative Guterman Test (1).

Case No.	Date	Guterman test	Aschheim-Zondek reaction
70	16/ 1/47	Negative	Negative

Comment (Group VI). In this case there were no signs of pregnancy, but after one period having been missed, bleeding started when the following period was due. Threatened abortion was suspected. This did not prove the case and the amenorrhoea was probably psychogenic.

DISCUSSION.

This is a preliminary report based on the findings and follow-up in 55 cases diagnosed clinically as threatened abortion, and therefore no conclusions can be drawn statistically from such a small series of cases.

However, the results of this investigation would tend to lend support to the following arguments:

Good results from progesterone therapy in threatened abortion can be expected only in the presence of progesterone deficiency, and provided the condition has not yet reached an irreversible stage. If, therefore, progesterone therapy is to be employed in these cases, a test to demonstrate the presence or absence of progesterone deficiency should be carried out before any progesterone is given empirically.

There is some reason to believe that the administration of progesterone in the absence of any natural deficiency may be followed by acceleration of the abortion.

The majority of cases of threatened abortion are not accompanied by evidence of progesterone deficiency—only 11 out of 39 cases gave negative Guterman test results.

In cases of threatened abortion unaccompanied by evidence of progesterone deficiency, the cause of the threat to the continuation of the pregnancy is more commonly not found (22 out of 28 cases), especially so if abortion does not follow.

The necessity for careful clinical examination in all cases is underlined by the fact that, if there is no progesterone deficiency, another cause for abortion must be sought; while if there is progesterone deficiency it may not be the only factor present favouring abortion.

The employment of simultaneous Guterman and Aschheim-Zondek tests helps to differentiate cases of corpus luteum cyst and of missed and complete abortion from cases of threatened abortion. In the present investigation the application of the information derived from the combined results was delayed by the length of time taken to complete the Aschheim-Zondek test. In some cases this resulted in the pointless administration of progesterone. The substitution of a more rapid gonadotrophin pregnancy test, such as the Xenopus or Friedman tests, would have avoided this difficulty to a large extent.

SUMMARY.

1. A series of 57 cases, diagnosed clinically as threatened abortion, were investigated by means of the Guterman test and 55 of these were followed up.

2. The Guterman test is a rapid, practical and economical method of distinguishing those cases of threatened abortion which are accompanied by progesterone deficiency (as reflected in the urinary pregnanediol excretion), and which therefore are likely to benefit from progesterone therapy.

3. There is some reason to believe that the administration of progesterone in threatened abortion unaccompanied by progesterone deficiency, may accelerate abortion.

4. The simultaneous performance of the Guterman test and a rapid gonadotrophin pregnancy test may differentiate other conditions, notably corpus luteum cyst, from threatened abortion.

APPENDIX A.

THE TECHNIQUE OF THE GUTERMAN TEST.

A. *Hydrolysis and Extraction of Pregnandiol.*

1. 100 ml. urine (first morning specimen), 50 ml. toluene, 10 ml. concentrated hydrochloric acid, and two glass beads are added to a 500 ml. flat-bottomed Florence flask.

2. The flask is connected *via* a one-holed cork stopper to a vertical Leibig condenser (water-cooled, 400-500 mm. length jacket) and the mixture is boiled vigorously over an electric hotplate for 15 minutes.

3. The flask and its contents are brought to room temperature by cooling under the water-tap.

4. The mixture is transferred to a 500-ml. separatory funnel and the lower layer (urine) is drawn off.

5. The toluene layer and emulsion are washed twice with 15-ml. portions of N/10 sodium hydroxide and then twice with 15-ml. portions of distilled water.

B. *Precipitation of Impurities.*

1. The washed toluene and emulsion (A-5) are transferred to a 125-ml. Erlenmeyer flask with two glass beads.

2. The mixture is boiled over an electric hotplate (in the hood).

3. When the water has evaporated and the toluene mixture is boiling smoothly, 10 ml. of 2 per cent sodium hydroxide in absolute methanol is added (see note 1 for the preparation of this solution).

4. The mixture is evaporated until a granular precipitate appears and one half of the original toluene volume is reached.

5. The toluene mixture is then filtered while hot through a fritted glass filter (medium porosity, Pyrex) with mild suction. If the filtrate has an orange pink or brown tinge, B-3, B-4 and B-5 must be repeated until the filtrate is yellow or yellow-green.

6. The precipitate of B-5 is washed with 15 ml. hot toluene.

7. The combined filtrates of B-5 and B-6 are evaporated to dryness over the hotplate (in the hood), a gentle stream of air being used to drive off the last traces of toluene. This avoids charring of the residue.

C. *Precipitation of Pregnanediol.*

1. Acetone 5 ml. is added to the residue (B-7) and the mixture is warmed over a hotplate until the solution is complete.

2. N/10 sodium hydroxide 20 ml. is added slowly and the mixture is brought just to boiling on the hotplate.

3. The flask is then placed in a refrigerator (5°C.) for 1 hour. For quantitative recoveries it is preferable to refrigerate overnight.

D. *Isolation of Pregnanediol.*

1. The mixture C-3 is filtered through a fritted glass filter with mild suction.

2. The precipitate is washed with 15 ml. distilled water.

3. The receiving flask is changed, and 10 ml. hot absolute alcohol is passed through the fritted glass filter to dissolve the precipitate.

4. The alcohol filtrate (D-3) is evaporated to dryness from the receiving flask over an electric hotplate (in the hood).

E. *Colour Development.*

1. Ten ml. conc. sulphuric acid is added to the residue (D-4) and the colour is observed in the flask when solution is complete. Colourless to light yellow solution is read as negative. Deep yellow to orange and orange-brown is read as positive.

Note 1. Preparation of the 2 per cent sodium hydroxide in absolute methanol solution.

1. Sodium hydroxide pellets are dissolved in absolute methanol in a dry Erlenmeyer flask to a concentration of 4-8 per cent.

2. The mixture is filtered through a *dry* sintered glass filter to remove the precipitated carbonate.

3. The sodium hydroxide concentration of the filtrate is determined by titration with N/10 sulphuric acid.

4. The filtrate is then adjusted to a concentration of 2 per cent with absolute methanol.

5. The solution is freshly prepared every week. *Note 2.*

New reagent solutions should be tested for their production of spurious colours. Each solution, in the volume employed in the test, is evaporated to dryness in the hood. Ten ml. concentrated sulphuric acid is added to the cooled residue of each solution. If a colour reaction is obtained, the reagent must be discarded.

APPENDIX B.

Quantitative Method of Pregnanediol Assay.

1. Make a solution of pure pregnanediol (melting point 235-7°C.) in warm absolute alcohol so that 1 ml. of the solution contains 0.2 mg. pregnanediol.

2. Take aliquots of 1 ml., 2 ml., 3 ml., 4 ml., 5 ml., 6 ml., 8 ml., and 10 ml. of the solution in separate test tubes and evaporate each to dryness in a water-bath. Allow to cool.

3. Add 10 ml. concentrated sulphuric acid to each residue. Eight colour-strengths will thus be obtained.

4. From these 8 solutions draw a calibration curve, measuring colour intensity in a Spekker photo-electric absorptiometer using an Ilford No. 601 blue filter. The strength of the solution is plotted against the drum reading of the absorptiometer.

5. After obtaining its drum reading on the absorptiometer, the strength of an unknown solution (E-1 of the Guterman test) may be read directly from the calibration curve.

Note. Use the same bottle of concentrated sulphuric acid for making the test known-strength solutions and for adding to the isolated pregnanediol when performing the Guterman test (E-1). This involves making a new calibration curve whenever a new bottle of the acid is opened.

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An Investigation of the Causes of Sterility and Lowered Fertility in West African Negroes

BY

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The problem of sterility and fertility is second in importance only to that of self-preservation. It is not surprising, therefore, that references to the subject are to be found in literature since man first acquired the art of writing.

In the Bible several references are to be found. The Mosaic laws give strict regulations for the control of venereal disease, and the abstinence from intercourse for 7 days after the cessation of the menstrual flow ensures that in the majority of cases it occurs during the "mid-cycle", which we now know is the most likely period for fertilization to occur. Kurzrok (1928) has pointed out that this law is occasionally responsible for sterility in women with short menstrual cycles, or whose menstrual loss is continued for long periods.

The story of Jacob and Rachael well illustrates the distress which sterility may cause and also the reluctance of the male to admit any responsibility for it:

"And when Rachael saw that she bare Jacob no children, Rachael envied her sister, and said unto Jacob 'Give me children or else I die.'

"And Jacob's anger was kindled against Rachael and he said ' Am I in God's stead, who hath withheld from thee the fruit of the womb ?'."

Hippocrates (460–370 B.C.) recognized that uterine displacements, menstrual disorders and excessive fat were associated with sterility in women. For treatment of sterility, he recommended cleanliness, local treatment of the cervical os and, for tamponage, it is interesting to note that, among other ingredients, he mentions sodium carbonate. The value of *coitus a tergo* in uterine displacement was appreciated by the Ancient Greeks. Aristotle was aware of the importance of male sterility and especially mentions drunkards, invalids and old men. The Chinese physicians, too, appreciated the importance of male sterility and instance as causes excessive intercourse, arsenic and mercury (Ploss and Bartels, 1935).

Although the ovary was discovered by Herophilus in 300 B.C., it was not until 1672 that the significance of the ovarian follicle and the ovum was shown by De Graaf. Other milestones were the discovery of the spermatozoids by J. Ham and Leeuwenhoek in 1677, and Spallanzani's proof in 1768 that the spermatozoa were the active fertilizing agents. In 1889, Jaggard taught that anovulatory menstruation was a probability, but scientific proof of this supposition was not forthcoming until 1934 (DeLee, 1938).

It is only in the last quarter of a century that significant progress regarding the investigation of sterility has been made. Rubin (1920) demonstrated a simple method of testing tubal patency, and in the following year Huhner (1921) introduced the post-coital test. The work of Meyer (1913, 1920), Schroeder (1913a, 1919, 1928), Shaw

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(1925), Frankel (1910), Novak (1926) and others have established the significance of the menstrual cycle. In 1925 Evans and Burr demonstrated the importance of vitamin E as a factor in the sterility of animals. In 1923 Allen and Doisy isolated the hormone oestrin, and Hisaw (1930) progesterone. Wiesner and Crew (1929) and Aschheim and Zondek (1928) working independently demonstrated the importance of the pituitary on the ovary, and postulated the presence of 2 separate hormones—prolan A and B—acting on it. Ogino (1928) and Knaus (1929) showed that ovulation almost invariably occurs in the mid-cycle.

With the increase of knowledge attained by these and many other workers, the complexity of the subject of sterility is yearly being more appreciated. All authorities now recognize that, in the majority of cases, the problem resolves itself into a number of infertile factors rather than one major factor responsible for sterility. Thus, the importance of a routine and scientific procedure in the investigation of these cases is now appreciated. Particular mention, in this respect, should be made of the work of Lane-Roberts, Sharman, Walker and Wiesner (1939), Williams (1944), and Meaker (1934).

Introduction.

This work was undertaken during an 18 months' military tour of Nigeria. The work in the first half of the tour, and almost exactly half the case-material collected, was undertaken in the coastal capital of Lagos, and the second half was undertaken in the large northern town of Kaduna. As well as a number of inpatients who were investigated, sterility clinics were held, at first weekly, and, as the demand grew, twice weekly.

The literature on the subject of sterility is now very large, and many new theories and refinements have been introduced even since the material for this paper was collected (October 1941 to March 1943). To analyze the literature of sterility is beyond the scope of this paper, and only subjects relevent to the comparison of sterility in white peoples and West Africans are, for the most part, considered.

Lane-Roberts *et al.* (1939) have stressed the confusion which has been caused by lack of clear definition of terms relating to sterility. It is, therefore, of some importance that a clear definition of terms should be stated at the outset:—

Primary sterility is defined as sterility occurring in a marriage of 2 years in which there has been no known conception.

Secondary sterility is defined as a marriage in which there has not, for 3 or more years, been born a viable child, but in which one or more conceptions have occurred.

Absolute sterility. This denotes that an absolute bar to conception exists in either partner.

Relative sterility. No absolute bar is found to conception, but one or more factors which might be responsible for sterility are found.

It is admitted that the 2 latter definitions are open to the criticism that so much depends upon the interpretation of the individual observer, but much of the subject matter of sterility is open to this criticism.

Two-hundred and three cases have been investigated. Seventy-three of these were cases of primary sterility and 130 of secondary sterility. An analysis of the cases does not reveal any striking differences between those seen in the south and those in the north. They are, therefore, considered as a whole. It should, however, be noted that the proportion of the tribes seen in the north is not a true representation of that region. For although the Hausa tribe

predominate in the north, they rarely attend modern hospitals, and hence the Yoruba and Ibo tribes, who have infiltrated to the north with the Europeans, still form the majority of the patients seen.

The circumstances under which the investigations were done did not permit of full investigation being undertaken in all cases. In none were facilities or the required technical ability available for hormonal investigations. Seminal investigations were limited to sperm counts, the presence or absence of motility and the recording of abnormalities such as pus and blood cells. X-rays (e.g. lipiodol injection for tubal patency) were severely limited by wartime restrictions. Also, it was not considered justifiable to ask the laboratories to undertake too many histological sections.

The language problem was not nearly as difficult as might be expected. Apart from those who spoke good English, "Pidgin English" and the help of a nurse interpreter proved satisfactory in the majority of cases. On the whole, histories were well given and the impression was that they were reliable. It was more difficult to obtain the co-operation of the patients to attend for examination, and this especially applied to the men. Hence most of the work was essentially gynaecological. However, as will be shown later, considerable indirect evidence was obtained about male fertility from the polygamous customs of the West African.

It was thought, when the investigation was started, that there would be considerable difference in the aetiology of cases of primary and secondary sterility, but on analysis, the findings in most instances were comparable. Hence it has been decided to submit the material collectively, and to refer to differences between the two groups only when the figures are sufficiently divergent to merit comment.

The customs of the natives and the local conditions are of such importance to this subject that although I fully appreciate that my knowledge of these matters is very limited, owing to the short duration of my stay in West Africa, some impressions at least must be recorded.

Women's status in West Africa is much inferior to that of the men. Marriage is largely a business deal and, the wealthier the man, the more wives he usually has. Wives are treated as servants, and to some extent as beasts of burden. Even the christians have often one christian wife and several others—non-christian. One of my military duties included the censorship of letters, and I was very interested to note that not once did "love" as we know the word in this country enter into any letter between a man and his wife. Terms of affection between two individuals appeared to be restricted to members of the same sex, and yet homosexuality, I believe, was extremely uncommon. Sex, and "love" appear to be separate entities to the West African.

There is no doubt, too, that sex-instruction and experience are treated in a very different manner in West Africa. Children at an early age are encouraged to have sexual experiences. Many cases of gonorrhoea were seen in children of 12 years and under, and if pregnancy results it enhances the value of the woman in the marriage market. It is not uncommon to see Miss X announcing with pride in the local newspaper that she has given birth to a son. On the other hand, after marriage, the wife at any rate does not have extra-marital intercourse.

The polygamous customs appear to suit the West African well. The first wife is anxious for her husband to get more wives, for she will then be mistress and the others servants. Also a single woman prefers a man with other wives, for then her duties will be shared and lessened. As well as

household duties the wives are expected to make or cultivate marketable products, and the husbands allow a proportion of their profits to be kept by the women.

Superstition plays a big part in the West African's life. Relative to this subject it may be mentioned that the men commonly believe that they are sterile unless they have had gonorrhoea, and operation has frequently been refused by women on the grounds that once the abdomen has been opened they will never again bear children.

Chivalry towards women does not exist. If there are heavy loads to be carried to and from market, it is the women who do the carrying whilst the husband walks alongside. All weights of any magnitude are carried on the head, and this and the other physical duties which are imposed upon the women give them a regal bearing and fine physique. In the Maternity Hospital at Lagos, there are some 3,000 to 4,000 deliveries per year. The women are usually up washing the babies within 2 hours of delivery, and the average duration of stay for a confinement is 24 to 48 hours. Uterine involution is rapid and genital prolapse almost unknown.

At the beginning of these investigations an attempt was made to determine the significance of tropical disease and past illnesses as a factor contributing to sterility. The attempt had to be abandoned; firstly, because it was found quite impossible to obtain anything like an accurate diagnosis from the histories and, secondly, because it would have entailed so much pathological work investigating all the patients that the work could not have been completed in the time available. Whereas it is true in this country that two diagnoses should not be made to account for symptoms if one will suffice, in West Africa it would be more correct to say that when one has proved that the patient has three or four diseases, one should not be satisfied until several

others have been excluded as being the major factor. Therefore, although it is fully appreciated that many tropical conditions may have a bearing on sterility, it was found impracticable to assess the significance of these factors, and only those factors comparable with European conditions are considered.

Diet in West Africa is good and abundant. The staple items of diet are yams, cereals, and an abundance of citrus fruits. Meat is probably scarce. Salt, even in the coastal areas, is scarce and salt rioting occasionally occurs. Malnutrition and deficiency diseases are uncommon. As regards the women there is little pelvic deformity and childbirth is usually easy. There is no doubt that the pithecord type of pelvis is much more common in West African women than in Europeans.

The general fertility of the West African is not high. It is rare for a woman to have more than 3 or 4 children, and the average is 2 or 3. In the Ibo tribe a contributory factor may be that one of their laws is that sexual intercourse is not permitted for 2 years after the birth of a child.

In nearly all the tribes encountered in this survey male circumcision was practised. In the Ibo tribe female circumcision was also performed in all women except those born into Christian families. The object of this ceremony could not be elicited and the conclusion reached was that if there ever had been any specific object in this operation it had long ago been forgotton. The Americans have revived female circumcision as a cure for female frigidity, but apart from the fact that the operation in the Ibo usually includes clitoridectomy, psychological frigidity in West African women appears to be unknown. The most probable explanation is that it is a mild form of vulval fibulation connected with the ensurance of virginity before marriage.

In no case of the present survey did this operation appear to have any bearing on sterility, although a case was seen of a woman married for 2 months in which the operation had extended to fibulation. The vulva was almost completely excised and the vaginal orifice would not admit the little finger.

Summary of Material Obtained.

Length of sterility. The average length of sterility in the primary cases was 6.7 years. In the cases of secondary sterility it was 7.9 years.

Age of patients. In view of the full menstrual, obstetric, and general histories which the patients were usually able to give, it is surprising that less than a third of them were able to state how old they were. Of those who knew their age, it was found that 75 per cent were 30 years of age or under. Sharman (1944) found that in 500 cases of sterility that two-thirds (66.6 per cent) were in the age group 20 to 30. It is perhaps surprising that the West African does not show an even higher comparable percentage of youth as early marriage is the rule rather than the exception. The explanation is probably to be found in the fact that the average length of sterility in this group is 7.44 years.

To estimate an African's age is not easy but, in order that an approximate idea of their age may be given, this has been estimated for the remainder. This was done from their appearance, length of marriage, the number of years since the menarche, etc. As the figures for the known ages tally closely with the above remarks, they will not be considered further.

Menstrual Histories.

Excluding 3 cases of primary amenorrhoea, 20 out of a total of 70 cases of primary sterility and 39 cases of secondary sterility out of 130 knew the age at which menstruation commenced.

The average age at which menstruation started in this total of 59 cases was 14.6 years.

In the 20 cases of primary sterility it was 15.2 years.

In the 39 cases of secondary sterility it was 14.4 years.

Ploss and Bartels (1935), among others, have shown that it is generally thought that menstruation in the African begins at an early age, and Morison (1943) attributed the above figures to the fact that they were sterile women in whom a later menstruation was to be expected. However, on a further analysis of the figures, it was found that in 25 women with secondary sterility, who had previously borne viable children, the average age at the menarche was 14.4 years. Although these figures are too small on which to base definite conclusions, it would appear that it is necessary to taken with reservations the common belief that the menarche commences early in the African, until further reports are available. Kark (1943) and Mills (1937) report similar findings in normal South African girls.

As regards the menstrual cycle it is considered that a variation ranging from 21 to 35 days is normal. Taking this as a basis, it was found that 12 patients with primary sterility and 27 patients with secondary sterility had abnormal menstrual cycles. These cases are subdivided as follows:—

Primary sterility: 12 cases.

	Cause found
3—Primary amenorrhoea	Endocrinal stigmata.
1—Secondary amenorrhoea	Severe ankylostome anaemia.
7—Hypomenorrhoea	4 Endocrinal stigamata. 3 Unexplained.
1—Polymenorrhoea	Unexplained.

Secondary sterility : 27 cases.

7—Secondary amenorrhoea	4 Various causes.
	3 Unexplained.
9—Hypomenorrhoea.	5 Endocrinal stigmata.
	3 Gross pelvic sepsis.
	1 Unexplained.
8—Polymenorrhoea	3 Gross pelvic sepsis.
	5 Unexplained.
3—Metropathia haemorrhagica	Functional.

Dysmenorrhoea in the West African is a common symptom. It was a complaint in no less than 122 cases (60.1 per cent). It was more common in cases of primary sterility (70 per cent) than in secondary sterility (55.4 per cent). Spasmodic dysmenorrhoea was relatively more common in primary sterility, although, in both, congestive dysmenorrhoea predominated.

An analysis of the findings is given below.

It will be seen from the above that in the majority of cases a sufficient clinical cause for the dysmenorrhoea was found, which is in contrast to the findings in the white races.

The Role of Gonorrhoea and Pelvic Infection.

The role which gonorrhoea and pelvic sepsis plays in the West African is derived from the history of gonorrhoea or vaginal discharge, congestive dysmenorrhoea, dyspareunia, history suggestive of salpingitis,

postabortal or puerperal fever, the tubal patency test, the findings of a pathological discharge and other clinical and operative evidence of pelvic infection. A tabulated summary shows the significance of these factors as a cause of sterility in the West African :—

	Per cent
History of gonorrhoea in women	18.7
History of gonorrhoea in men (79 cases)	72.3
History of vaginal discharge	67.5
History of congestive dysmenorrhoea	37.9
History of dyspareunia	29.2
History suggestive of pelvic infection	40.0
Pathological vaginal discharge	64.5
Clinical evidence of salpingitis	29.6
Proved gonorrhoea (148 cases)	13.5
Pus cells in cervical smear (148 cases)	58.8
Negative tubal patency (85 cases)	59.5
No evidence of gonorrhoea or sepsis in either partner	12.8

It becomes apparent at once on a consideration of these figures that gonorrhoea and pelvic sepsis in the West African are major factors in the aetiology of sterility. So usual is gonorrhoea that there is a common belief that the West African male is not fertile until he has had the disease, and several will give histories of having had anything from 15 to 20 re-infections.

Whereas only 18.7 per cent of the women gave a history of gonorrhoea, 72.3 per cent of the men gave such a history. This may

DYSMENORRHOEA: ANALYSIS OF FINDINGS

	Primary sterility.	*Secondary sterility*
Total complaining of dysmenorrhoea.	50 out of 73 (70 per cent)	72 out of 130 (55.4 per cent)
Spasmodic dysmenorrhoea.	20 cases :	22 cases :
	11 Genital hypoplasia.	4 Genital hypoplasia.
	1 Pelvic sepsis.	7 Pelvic sepsis.
	8 Unexplained.	1 Fibroids.
		10 Unexplained.
Congestive dysmenorrhoea	30 cases :	50 cases :
	22 Pelvic sepsis.	36 Pelvic sepsis.
	1 Genital hypoplasia.	3 Genital hypoplasia.
	4 Endometriosis.	2 Endometriosis.
	5 Unexplained.	1 Fibroids.
		9 Unexplained.

be due to the reluctance of the women to admit having had the disease, but it is far more likely that they do not recognize its symptoms. This suggestion is strengthened by the fact that 67 per cent of them give a history of vaginal discharge and a pathological discharge is found in 64.5 per cent, figures which are comparable with the histories given by men.

Comparable figures are difficult to find in the literature but Schofield (1935) states that gonorrhoea is an important factor in sterility in the East African. Levy and Meyer (1937) and Miller (1944) have shown that venereal disease is much more rampant in the American negro than in the white races. A comparison of the figures of other writers amply confirms that this is so too in the West African. Feiner (1942) found that in 5.8 per cent of cases of sterility there was a history suggestive of pelvic inflammatory disease (cf. 40 per cent present series), and he found clinical evidence of salpingitis in 4.7 per cent (cf. 29.6 per cent). Stein (1938) found an even lower figure (1 per cent) of salpingitis, but Suggs (1943) states that in 12 per cent of his cases he found chronic inflammation and adhesions.

So, also, a comparison of negative tubal patency tests in this series (59.5 per cent) with the published literature is revealing. Different authors' figures vary very considerably, but none approach this percentage. Stein (1938) found that in only 10 per cent were the Fallopian tubes not patent, Green-Armytage (1943) and Meaker (1934) give 14 per cent as an average figure, whereas Feiner (1942) (35.5 per cent) and Sharman (1944) (38 per cent) give a considerably higher figure of non-patency. Rubin (1942), in 3,380 cases, found that the Fallopian tubes were occluded in 29.1 per cent. Thus it would be reasonable to say that from the avail-available statistical results of tubal insuffla-

tion about one-quarter were found to be non-patent, a figure less than half of the present series.

In 84 patients tubal insufflation was undertaken. In 8 others it was attempted and proved a failure—usually due to scarring of the cervix. A modified Bonney apparatus without anaesthesia was used.

A further analysis reveals that in 30 (60 per cent) of the 50 patients in whom the tubes were non-patent, a clinically demonstrable pelvic infection was present. In 8 of these patients there was bilateral salpingitis. In 4, unilateral salpingitis and in the 18 other patients evidence such as fixed uterine displacements, tender bulky uterus, etc. It was somewhat surprising to find that in 12 (35.3 per cent) of the 34 women whose Fallopian tubes were patent there was also evidence of pelvic infection. In one (No. 139) there was apparently bilateral salpingitis. It must be conceded that this was probably an error of clinical diagnosis, but in 8 other patients there was evidence of unilateral salpingitis and yet the other Fallopian tube remained patent. Thus, although the proportion of cases with clinical evidence of pelvic sepsis is higher in the cases with a negative tubal patency, it is evident that clinical examination alone is an inaccurate gauge of the probability of tubal occlusion.

The question of undertaking tubal insufflations at all under the circumstances was approached with considerable trepidation. However, confidence was increased with the experience that in no case did it activate a latent infection. It was not undertaken if there was any clinical evidence of acute infection. Thus, if tubal patency tests had been undertaken in all cases, the proportion of those proving negative would probably have been higher. However, this factor is probably not of much importance, as it is rare to see a West African woman with evidence of acute

inflammatory disease. They appear to be able to acquire large inflammatory masses in the pelvis and abdomen with little or no apparent effect on their general health. This characteristic has also been noted by Miller (1940), and Levy and Meyer (1937) in American negroes and by Schofield (1935) in East Africans.

The significance of gonorrhoea in the aetiology of sterility is questioned by few, but its importance in the white races is obviously less than in the West African. It is not possible to say how often gonorrhoea results in sterility. Lane-Roberts et al. (1930) state that pelvic inflammatory disease is one of the commonest causes of sterility in women. Reynolds and Macomber (1924) say that gonorrhoea often results in complete sterility. The difficulty of obtaining bacteriological proof of gonorrhoea in women is also universally recognized. Lewis (1943) found only 6 positive results in 80 cases of inflammatory disease, and Mahony (1942) found 21 per cent of 1,598 prostitutes, suspected of harbouring gonorrhoea, to be positive. Miller (1944) states that, when tubal infection has occurred, it is rare to obtain bacteriological proof of the disease. Compared with these findings a positive percentage of 13.5 in 148 routine cervical smears is a high rate, rate, especially when it is taken into account that the vast majority of patients had only 1 cervical smear taken.

Schleyer (1943) found that in 6 women out of 10 who had been cured of gonorrhoea, the Fallopian tubes were closed 3 to 6 months after the infection. He was able to re-open 4 of these 6 with repeated insufflations. It would appear to be most unlikely that anything like the same proportion of West African women have their Fallopian tubes occluded by gonorrhoea, for if this were so the race would soon become extinct. Whether this is due to the undoubted mildness of the average infection in West Africa or that the tubal occlusion is only a temporary matter, it is not possible to say.

Postabortal and puerperal fever are of minor consideration in the aetiology of sterility in West Africa. In the total series only 7 reported any abnormality, one of these being postabortal and the remainder puerperal. In some of these cases it was difficult to be sure that the fever was not due to some other disease—particularly malaria. Puerperal fever was not encountered by me in West Africa and from discussions with other medical practitioners, it was confirmed that it is a rare disease. Also inquiries from several pathologists appeared to confirm that the haemolytic streptococcus is unknown in Nigeria, and this is probably one of the main factors in the virtual absence of puerperal fever.

It would appear, therefore, that pelvic infection in West African women is largely a result of gonorrhoea. But whereas gonorrhoea is responsible for a great deal of the sterility in the West African, there is evidence to show that each single attack of gonorrhoea has, on the average, not the same power of producing permanent damage as it has in the white races.

Genital Hypoplasia and Endocrinological Factors.

Although these factors are universally accepted as being of great importance in sterility, the difficulty—except in gross cases—is the practical evaluation of their significance. The American school (Lawrence and Rowe, 1928; Rowe, 1930; Haselhorst, 1933) consider that a detailed hormonal analysis is an essential part of the investigation of sterility, but Lane-Roberts et al. (1939) do not find these costly and technically difficult procedures to be of practical value as a routine investi-

gation, and found no abnormalities in 17 of 24 patients so examined. Furthermore, from the available figures of published results, it soon becomes apparent that one of the most important factors is the interpretation of the investigator. For example, in assessing cases of uterine hypoplasia, Feiner (1942) reports an incidence of 5.2 per cent; Stein (1938), 12.5 per cent; Suggs (1943), 32 per cent; and Meaker (1934), 42 per cent.

In the present series it was found that 39 women (19.2 per cent) showed stigmata of maldevelopment or severe genital hypoplasia. As would be expected this condition was more common in cases of primary sterility (37 per cent) than in cases of secondary sterility (9.2 per cent). Of the 12 patients with secondary sterility, half had had 1 early abortion only. Only gross and easily demonstrable cases of hypoplasia were included in this series, and the impression gained was that faults of development were very much more common in the West African than in the white races. As examples:

CASE No. 17 (Fig. 1). Estimated age 20. Married 2 years. History of primary amenorrhoea. Breast development had occurred 6 years ago and for the last 3 years she had had lower abdominal pain at monthly intervals. *Examination.* General appearance very depressed. Height 5 feet. Weight 9½ stones. Well marked breast development. Fat inclined to male distribution. Pubic hair scant. The vulva was moderately well developed anteriorly but deficient posteriorly (Fig. 2). The vagina was represented by a depression one inch deep, at the vault of which was firm scar tissue. *Per rectum*: uterus not felt. Left ovary palpable.

November 28th, 1941. Exploratory laparotomy. Both ovaries were found to be well developed, the left containing many follicular cysts. There were symmetrical bicornuate uteri 4 inches long, and the Fallopian tubes appeared to be of normal development. The distal ends of both uteri terminated in thin cords of fibrous tissue, meeting in the mid-line. The cervix was represented by fibrous tissue some ¾ of an inch in diameter. Left salpingo-oöphorectomy was performed. With the abdomen still open, the patient was then placed in the lithotomy position, and silkworm guide sutures were passed from the vaginal dimple below to the cervix. Sections of the left Fallopian tube and ovary proved to be normal.

December 28th, 1941. Vaginal exploration. After cutting through ¾ of an inch of firm fibrous tissue, a septate vagina about 2 inches long was encountered. The septum and fibrous tissue were excised, and the reconstituted vagina now comfortably accommodated a medium sized Ferguson's speculum.

CASE No. 33. Aged 36. Primary sterility. Primary amenorrhoea. Coitus has been possible but always difficult and painful. Married 7 years. *Examination.* Height, 5 feet 6 inches. Weight, 16½ stones. A very stout woman but alert and energetic. No other stigmata of hypothyroidism. Breasts undeveloped. Abdomen very fat, otherwise normal. Clitoris and labia undeveloped. No pubic hair. The vagina would admit 2 fingers with difficulty, was 2½ inches long, narrowing at its vault to the cervix, which was minute. No uterus could be detected on vaginal or rectal examination.

CASE No. 116. Height, 5 feet 6 inches. Weight, 9 stone. Estimated age 20 years. Married 3 years. Primary sterility. Menstrual cycle normal, with moderate dysmenorrhoea first day of menstruation. No history of gonorrhoea, but vaginal discharge 5 months. No dyspareunia. Husband has one child aged 2 years by other wife. *Examination.* Good physique. Breasts large. The labia minora were attached to each other over an area of ½ an inch at the junction of their anterior and middle thirds. This appeared to be a congenital failure of complete canalization, as there was no scarring or other indication that it was a secondary fusion of the labia. The patient was unaware of anything abnormal. Two fingers could be admitted easily into the posterior compartment of the vagina so formed. Vagina, cervix, uterus and adnexae were normal.

Ide-positive. Endometrium showed well-marked luteal reaction (28th day cycle). *Cervical smear*: some pus cells. No gonococci.

CASE No. 166. Aged 27. Stout. Married 3 years.

Primary sterility. Menarche at 16. Regular cycle of 28 days until marriage, when the cycle varied from 24 to 30 days. Loss for 2 to 3 days. Scanty since marriage. Slight pre-menstrual dysmenorrhoea. *Examination.* Breast development and general body configuration normal female. Moderate under-development of the external genitalia. Clitoris circumcised. Vagina will admit 2 fingers with difficulty. The cervix felt irregular, and on speculum examination was found to consist of 2 distinct and separate cervices. A probe entered both cervices, but could be inserted only 2 to 2½ inches. Tubal patency in both cervices was negative at 200 mm. Hg. Bimanually there appeared to be a uterus bicornuis, and a swelling, the size of a golf ball, was palpable in the left fornix.

Unfortunately, this patient failed to report for uterosalpingography as requested.

CASE No. 201. Aged 20 (estimated). Married 3 years. Primary sterility. Complete amenorrhoea, except that she states she had very slight vaginal bleeding 6 months ago. *Examination.* Immature breast development, but normal female contours, and pubic hair. External genitalia markedly underdeveloped. Vagina will admit one finger only, and is not more than 1½ inches long.

The cervix and uterus could not be felt on bimanual examination.

Information obtained from other practitioners in West Africa, as well as the above illustrations, undoubtedly suggests that all degrees of genital maldevelopment are relatively common in the West African.

It may be argued that 19.2 per cent of hypoplasia in the total series and of 37 per cent in cases of primary sterility does not show any appreciable increase of genital hypoplasia as compared with the white races, especially if the figures of Suggs (1943) and Meaker (1934) are considered. However, it must be remembered that a very high proportion of the total series are sterile on account of gonorrhoea in one or both partners, and that if these cases were eliminated, a much more comparable figure would be obtained. For instance, in only 20 patients with primary sterility can the likelihood of gonorrhoea being a factor be eliminated, and, of these, 13 show stigmata of gross genital hypoplasia, giving a percentage of 65.

Breast development, distribution of fat and pubic hair are usually considered to be of some significance as stigmata associated with endocrinal dysfunction in women. In this series, the significance of these factors appears to be slight or nil. The one possible exception is that, in 8 women, genital hypoplasia was associated with immaturity of breast development. However, there were 13 cases in which breast development was immature and there was no associated genital hypoplasia, and in 23 cases of hypoplasia there was no associated immature breast development. There was no apparent correlation between fat distribution, pelvic contours and genital hypoplasia. In the West African woman male distribution of pubic hair is common and was noted in 44 cases (21.7 per cent). Scant pubic hair seems to be of some endocrinological significance, but male distribution appears to be of no significance as regards sterility, and was noted with equal regularity in the antenatal clinics.

The Role of the Cervix.

Modern literature stresses the importance of the cervix and its secretions in sterility. Green-Armytage (1943) points out that the cervical secretions, at the time of ovulation, become particularly amicable to the reception of spermatozoa: The pH rises to 8.5, the secretion becomes rich in mucin and glycogen and the temperature of the canal rises. He believes that contraception and coitus interruptus interfere permanently with these factors. Lane-Roberts *et al.* (1939) and Van de Velde (1934) stress the importance of skilled courtship in releasing

cervical secretions amicable to fertilization, but consider that the position of the cervix is an even more important factor. Levy and Meyer (1937) give some very conclusive figures showing that endocervicitis and cervical lacerations are about 3 times as common in the white races as they are in the black. Schofield (1935) considers endocervicitis an important factor in sterility, as also does Gardner (1943).

In the present series abnormalities of the cervix were noted as follows: 45 cases of cervicitis associated with lacerations; 9 cases of cervical erosion; 26 cases of infantile cervices; 1 each of the following: prolapse, absence, double cervix, polypus.

Although, in the cases of cervical laceration, it was uncommon to find injuries as severe as are often seen in white persons, the amount of scarring and stenosis was often considerable. In the 92 parous patients who had produced full time foetuses, 48.9 per cent had cervical lacerations. This is appreciably more that the figure of 25.5 per cent for blacks given by Lévy and Meyer (1937), but considerably less than the figure of 74.5 per cent which they found in the white races.

Apart from demonstrable clinical lesions of the cervix, further evidence of infection was found in routine examination of cervical smears in 148 patients. As already considered, 13.5 per cent of these had proved gonorrhoea. In 87 patients (58.8 per cent) pus cells were present in the cervical smears and in half of these cases the infection was severe, as judged by there being more than 3 pus cells per high-power field. In many of these, the number of pus cells was very great.

Thus it would appear that cervical lesions play a very considerable role in the aetiology of sterility in the West African, although cervical lesions follow-ing childbirth are not so common as in white persons.

Anovulatory Menstruation.

Since Meyer (1913; 1920) and Schroeder (1931a, b; 1928) first scientifically investigated the menstrual cycle, a considerable amount of literature on the subject has accumulated and it is now possible to assess, to some extent, the significance of anovulatory menstruation as first investigated by Novak (1934) and Tietze (1933). Green-Armytage (1943) considers that, in 5 to 10 per cent of women who are sterile; this is probably the important factor, but like others, points out that it is not uncommon for women to have 1 or 2 anovulatory cycles every year. Sharman (1944) in 358 cases found that 11 showed periodic anovulation and 12 persistent anovulation. Only 2 of these 23 patients subsequently became pregnant. Roch, Bartlett and Matson (1939) consider that 4 per cent of cases of sterility are due to anovulation. Effkemann (1939) gives the higher figure of 14 per cent, whereas Williams (1940) found that 17.0 per cent of cases did not ovulate.

In the present series endometrium was obtained for histological examination in 24 cases either by biopsy or curettage. Five of these are disregarded for the present purposes as they were submitted to this investigation for reasons other than anovulation. Out of 19 cases 18 showed normal luteal endometrium, and 1 anovulation on the 25th day of a 30-day cycle (No. 122). The figures are too small from which to draw any definite conclusions but, from the small figures available, it would appear that the incidence of anovulation is comparable with the published figures.

Endometriosis. Endometriosis is difficult to diagnose with any degree of certainty from clinical findings and the history alone, but in many of these cases it was

suspected. In 3 cases it was found at laparotomy and was proved histologically. As only 8 laparotomies were undertaken in the series it strengthens the impression gained that endometriosis is a not uncommon disease in the West African.

Most authorities are agreed that endometriosis is usually associated with sterility. Caffier (1941) found that, in two-thirds of the cases of non-tubal patency upon which he operated, the occlusion was due to adenomyosis. Gardner (1943), however, states that the Fallopian tubes are often patent and that the patients may become pregnant. In the 3 cases of proved endometriosis 1 was found to have patent tubes, in another they were non-patent, and the third case was not tested.

Tuberculosis endometritis. Since these investigations were undertaken, Sharman (1944) has reported an appreciable (5.1 per cent) incidence of tuberculous endometritis discovered on the histological examination of endometrial biopsy specimens. No evidence of a similar nature was found on a re-examination of the 24 endometrial specimens in the present series.

Abortions. Abortions in the West African appear to be as common as they are in the white races. Out of 130 women with secondary sterility 60 had abortions, of whom 37 had had more than one abortion.

It is difficult to assess the importance which syphilis plays in producing abortions in the West African. The Ide test, which, for technical reasons, largely replaces the Wassermann and Kahn tests, is, among other conditions, positive in cases of yaws, encephalitis lethargica and certain phases of malaria. The Ide test was taken as a routine in all cases of admission to the Kaduna hospital. Of the 5,000 most recent admissions it was found that almost exactly one-third were positive. In the present series, out of 44 unselected cases, the Ide test was found to be positive in 22 cases (50 per cent). In those who had a positive Ide test 11 (50 per cent of positives) had had abortions, whereas among the negative Ide cases only 5 (22.7 per cent) had had abortions, suggesting that syphilis may be a factor in the occurrence of abortions in West Africans. Levy and Meyer (1937) have shown that syphilis is more common in the American negro, and although there is little doubt that this, too, applies to the West African, for the reason given, it is not possible to give conclusive proof of this.

There were 8 cases of habitual abortion, in which the patients had had 3 or more abortions without any viable pregnancies.

CASE No. 8. Yoruba tribe. Aged 35. Married 13 years. Height, 5 feet. Weight, 7½ stone.

Menstrual history. Menarche late (? age 20). Normal cycle of 30 days with 5 days loss. During the last 7 years, has had severe premenstrual dysmenorrhoea for 3 days. No dyspareunia. Libido poor, but intercourse occurs about twice a week.

Past history. Gonorrhoea in 1936. No symptoms now.

Obstetric history. Has been pregnant about 10 times, but on each occasion has aborted at 2½ to 3 months. The foetus was sometimes seen.

Examination. Poor physique; thin; breasts lax; male tendency to distribution of fat, pubic hair and pelvic outline. Pelvic organs normal except for a pinhole os, which would not admit the endometrial-biopsy curette. Cervical smear: Many epithelial cells and some pus cells. Numerous mixed organisms, but no gonococci. One morphologically normal spermatozoon seen. Ide test negative on 2 occasions.

In January 1942 this patient again aborted in the hospital at 2½ months, in spite of inpatient treatment, morphia, corpus luteum extract and Antuitrin "S" therapy. Unfortunately, she had been bleeding for 3 days before she reported.

In 3 cases it was thought that uterine retroversions might be a factor in the repeated abortions (Cases No. 14, 29 and

114). In Case No. 29 a ventrisuspension operation was performed, as in West Africa I was struck by the number of patients who had successfully had children following this simple procedure. In Case No. 114, the patient reported haemorrhage at the 4th month of pregnancy. The retroversion was replaced, maintained with a Hodge pessary, and the pregnancy was known to be progressing satisfactorily at the 6th month. This patient also had a positive Ide reaction and was given treatment. Case No. 69 had severe rectal lymphogranuloma inguinale and eventually died of peritonitis, but this was unconnected with her habitual abortion, as the most recent abortion had been 14 years before. Case No. 177 had developed metropathia haemorrhagica. In cases 35 and 47, no abnormality was found.

Uterine myomata. Fibroids, even sufficiently small not to interfere with pregnancy, are known often to be associated with sterility, and Shaw (1936) points out that myomectomy is often followed by pregnancy in a sterile woman.

In this series 8 cases were diagnosed as having uterine myomata. In no case was the diagnosis confirmed at laparotomy, and it is usually extremely difficult in the African to be sure of the diagnosis. For instance, in 2 other cases in which a diagnosis of fibroids was made pre-operatively, the swellings at laparotomy were found to be painless adnexal inflammatory masses adherent to the uterus. My own experience was that fibroids appeared to be considerably less common in West Africa than at home, but other surgeons with more experience thought that the incidence was approximately similar, although none gave the opinion that they were more common.

The figure of 8 myomata in 203 cases compares with other published statistics in cases of sterility in the white races. Stein (1938) reports 7 cases of fibroids in 200

cases of sterility, and Suggs (1943) reports an incidence of 3.5 per cent. Feiner's (1942) figures, however, are considerably less, and he found only 8 cases in 706 patients.

Levy and Meyer (1937) gave some very extraordinary and conclusive statistics for the incidence of fibroids in the American black races as compared with the white. They found that fibroids were about 7 times as common in blacks, and that whereas in them 16.5 of all admissions to hospital were on account of fibroids, in the white races the incidence was 2.5 per cent. Other American authorities agree that fibroids are much more common in the American negro. As the American negro originally came from West Africa, it would be interesting to speculate what factors are responsible for the divergence of these findings. Diet, modes of life, and psychological factors are probably of considerable importance.

Psychological factors. The psychological factors in sterility, which have received so much attention in European and American literature, are comparatively insignificant in the West African. This is due to the attitude which the West African has to sex. It is true that in some instances contact with western civilization and Christianity has introduced psychological barriers, but this factor is not yet of much importance. Their average attitude towards sexual matters is straightforward and open.

It is true that, in this series, a high proportion of women (29.2 per cent) gave a history of some degree of dyspareunia, but in the majority of cases (65 per cent) an adequate physical cause to account for this was found. No case of vaginismus was encountered. Wittkower and Wilson (1943), have shown the importance which psychological ill-adjustment can play in the aetiology of sterility, and although no

comparable investigations were undertaken, there is no doubt that these factors are not of equal significance in African women.

Male impotence is by no means uncommon in the West African. This is, however, almost invariably due to an organic cause such as sexual excess, alcoholism, syphilis or malaria. In the series under consideration, there was no complaint made of impotence. Lane-Roberts *et al.* (1939) report that it is not uncommon for men to think that they are potent and their impotence is only discovered when they are asked to provide a seminal specimen and no fluid is found in the receptacle. No similar instance was found in the West African. Even such a gross case as No. 4, in which the husband gave a history of gonorrhoea, was found to have epispadias, atrophic testicles and complete azoospermia, nevertheless produced 1.5 ml. of semen for examination.

The male responsibility as a factor in sterility. In recent years the male responsibility as a factor in sterile mating has been more and more recognized, and it is now fully appreciated that the investigation of sterility requires the examination of both partners.

Lane-Roberts *et al.* (1939) point out the extraordinary divergence of published reports on the responsibility of the male in cases of sterility, and attribute this to the reports in some instances being made by gynaecologists, in other by urologists, etc., each tending to stress the importance of their own investigations. Furthermore, they have shown that the results are largely a matter of the opinion of the observer, and the accuracy and technique of the investigations which he undertakes and their interpretation. It has now been generally agreed that the numbers and motility of sperms alone are insufficient evidence of male fertility (Lane-Roberts *et al.*, 1939; Walker, 1946; Seymour, 1939; Moench, 1939; etc.). Abnormal head forms and other factors must be taken into consideration. In spite of this, as recently as 1936 DeLee and Greenhill state, regarding Huhner's test, that "if numerous motile spermatozoa are seen, one knows the husband is satisfactory."

Whitehouse (1935) estimates in 20 to 25 per cent of cases of sterility the male is responsible. Nurnberger (1920) considers that in one-third of the cases the male is absolutely responsible and in another third partially responsible. Other reports are: Meaker (1934), 30 per cent; Crossen and Crossen (1941), 30 to 48 per cent; Sharman (1944), 31.6 per cent; Gardner (1943), 40 per cent; Joel and Kenyon (1941), 46.5 per cent; and Williams (1943), 30 per cent. Thus, considering the combined opinion of these authorities, it can be said that the male is responsible for sterility in from one quarter to half the cases.

In the present series it was not possible to undertake detailed seminal examination and, as Schofield (1935) found in the East African, the West African husband was often unwilling to attend for examination. On the other hand, the polygamous practices of the West African give data of considerable value. In spite of the advances which have been made in recent years in the elucidation of male sterility and fertility, the ultimate biological test of fertility is still a more accurate criterion than any laboratory test. The obvious criticism of evaluating male fertility by this method is that there can never be any absolute proof that the husband was responsible for any fertile coitus which occurred. My own impression, however, confirmed by some (and not by others), is that West African women do not have extramarital intercourse after marriage. If there is an appreciable error in estimat-

ing male fertility by this method, it will always be in favour of the husband, as it can be assumed that he has regular intercourse with any wives he may have.

Another difficulty is to arrive at a standard of biological fertility. For example, a man who has several children with 2 or 3 wives cannot necessarily be considered biologically fertile unless he has been responsible for a pregnancy within the last few years. So also, a man with several wives and no-children cannot necessarily be considered biologically sterile if one of his wives has recently become pregnant. The standard adopted for biological fertility in this paper is that at least 1 of 2 or more wives has had a pregnancy within the last 2 years. As regards standards of fertility from seminal examinations, this is based entirely on the numbers of spermatozoa and their motility. Summarizing the evidence of male fertility and sterility, the following data are available:

(1) Thirty-five cases were willing to submit themselves to clinical examination. Eighteen abnormalities were found in 14 patients:

Bilateral testicular atrophy or immaturity, 10 (28.6 per cent); gumma of testis, 1; spermatocele, 1; chronic epididymitis, 1; epispadias, 1; active gonorrhoea, 2; soft sores, 2.

Compared with abnormal clinical findings in the white races there is no doubt that the incidence of abnormalities found is high. Jeffcoate (1946) found that 26 men out of 208 examined (12.5 per cent) had bilateral testicular atrophy or hypoplasia— as compared with 28.6 per cent of this series. In 8 of the 10 cases of testicular atrophy or immaturity the patients gave a history of gonorrhoea, but it is doubtful whether gonorrhoea ever is itself responsible for this condition. In 6 of these cases seminal examinations were undertaken. In

3 there was complete azoospermia, in 1 marked oligozoospermia with numerous pus cells, and 2 were normal. In the case of gumma of the testis (No. 94) and in the spermatocele (No. 167) there was also azoospermia.

In view of the prevalence of gonorrhoea, it is surprising to find only 1 case with evidence of chronic epididymitis. Reynolds and Macomber (1924) found that gonococcal epididymitis occurred in 20 to 30 per cent of all cases of gonorrhoea in men. Thus the picture in the West African is again, in this instance, very different.

(2) In 43 patients, seminal examinations were undertaken. The analysis of the results was as follows:

Satisfactory (numbers of spermatozoa and motility) 31. Azoospermia, 10. Extreme oligozoospermia, 2.

Thus in 12 cases (27.9 per cent of cases) the male was found to be certainly sterile and, by modern methods of evaluation, this percentage would certainly have been higher. Suggs (1943) found that 8 per cent of 96 cases had azoospermia, Williams (1940), 10 cases out of 176 (5.7 per cent), Jeffcoate (1946), 9 per cent, compared with 23 per cent of this series.

(3) As regards biological fertility and sterility in men, taking the standard already defined, evidence was available in 113 cases:

Biologically fertile, 70 cases.

Biologically sterile, 43 cases (38.1 per cent).

(4) In some instances evidence of fertility or sterility is available from both the seminal examination and biologically. In others only one factor is available, and in others neither. Summarizing this evidence:

(1) Seminally fertile	14 cases	
(2) Biologically fertile	55 cases	83
(3) Seminally fertile Biologically fertile	14 cases	

(4) Seminally infertile ⎱
      Biologically fertile   ⎰   1 case

(5) Biologically infertile   33 cases

(6) Seminally fertile ⎱
      Biologically infertile ⎰   7 cases ⎬ 52

(7) Seminally infertile ⎱
      Biologically infertile ⎰   3 cases

(8) Seminally infertile   8 cases

(9) No evidence available   68 cases

Thus in 135 cases in which evidence of male fertility or sterility is available, 52 (38.5 per cent) show evidence of infertility or sterility. In 1 man (No. 202), the seminal examination showed azoospermia, and yet another wife had had a child 2 years ago. Either his sterility must have been acquired during that time, or else the child cannot have been his. In 7 cases the male was seminally fertile and yet biologically infertile. Several interpretations may be placed on these findings, but the following appear to be the most probable:

(1) The women were sterile (probably gonorrhoea) but the male was not.

(2) A more detailed examination of the semen might have shown infertility factors, although it should be noted that the majority of these patients had at some time had children, although not within the last 2 years (Nos. 9, 41, 49, 106, 131, 139 and 200).

Thus it may be concluded that the male partner in a West African marriage is in many cases responsible for sterility. The considerably higher proportion of cases with azoospermia suggest that his responsibility is even greater than in the white races. The biological test also shows how much he is implicated.

The clinical picture as a whole. One of the problems in assessing sterility is that there are so many factors involved that it is difficult to give a composite picture and compare the findings with other writers. So far, each individual factor has, as far as possible, been analyzed and the results compared with those of others. It is felt that a truer picture of the whole is obtained if a few typical cases are cited.

CASE No. 4. Height, 5 feet 6 inches. Weight, 7½ stones. Estimated age, 25. Married 5 years. Four years ago delivery of a full-time female child which died when 15 days old. Puerperium normal. No other pregnancies. Menstrual cycle has been a 17-day one for last 6 months. Before that 25-day. Average loss for 3 days. No dysmenorrhoea or dyspareunia. Libido fair but intercourse takes place only about 3 times per month. States she has not had gonorrhoea but a vaginal discharge has been present for 3 years. *On examination.* A thin, apathetic, ill-looking woman. Breasts—lax. Pubic hair and fat distribution—male tendencies. Clitoris and labia small. Cervix multiparous, elongated, very posterior and tender. Uterus—rather small. No swelling felt in fornices, which were tender. Thick white vaginal discharge. Cervical smear—pus cells +, epithelial cells +, numerous mixed organisms. No gonococci seen. Husband—has no other wives. History of gonorrhoea 4 years ago and occasional stinging pain on micturition still. Secondary sex characteristics normal.

Penile epispadias. Testicles small. Seminal examination—1.5 ml. semen. Azoospermia. Seven to 8 pus cells per high-power field.

Comment. A typical West African case of sterility. The azoospermia is a complete cause of sterility, but there are many other factors which might be responsible if this one factor had not made further investigation useless.

CASE No. 13. Yoruba tribe Age 30. Height 5 feet 2 inches. Weight 12 stone. Married 10 years but only 1 year with present husband. Primary sterility. Menstruation did not start until she was 20 but has been normal since. Slight abdominal pain after intercourse, which occurs about twice weekly. History of gonorrhoea 4 years ago. (Not with present husband). Complains that for some time she has been troubled with intestinal worms.

On examination. She was a large, stout woman. Nothing abnormal was found in the pelvis. The cervix would not admit the endometrial curette.

FIG. 1.

CASE No. 17. Uterus bicornis, semi bicollis. Note
the well developed breasts, scant pubic hair and
absence of female pelvic contour.

FIG. 2

CASE No 17   Note the normal development of the
vulva anteriorly and its deficient development
posteriorly.

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Cervical smear—Numerous epithelial cells, no pus cells, mixed organisms +,+, no gonococci. The husband was aged 36, of good build and had 5 children by other wives, the youngest 3 months old. On clinical examination he was normal.

The patient's stool was heavily infected with ova of ascaris and she was given 2 treatments with chenopodium and magnesium sulphate mixtures. Soon after this she missed a period—3 weeks overdue—but then aborted. A month later the Fallopian tubes were tested and found patent.

Comment. This is apparently a case of a woman 10 years sterile who became pregnant after worm treatment. The taking of the cervical smear and the attempt to pass the endometrial curette may have been factors in assisting impregnation. Her subsequent history is unknown.

CASE No. 26. Aged 28. Primary sterility for 8 years. Menarche aged 15. Cycle 28 to 30 days. Loss 4 to 5 days,- excessive. No dysmenorrhoea but severe breast pains for 10 days premenstrually. No dyspareunia, but complains of seminal efflux after intercourse (a common African complaint and associated by them with sterility). Intercourse occurs about twice per week. Past history, severe abdominal pains for 1 month in 1930. No history of gonorrhoea or vaginal discharge. *Examination,* November 29th, 1941. General physique good. Breasts small. Pin-hole elongated os. Left ovary enlarged. Dilatation and curettage: probe entered cervix with great difficulty. Fallopian tubes not patent (24th day cycle). Endometrium showed well-marked secretory phase of menstrual cycle.

The husband has 1 other wife now pregnant and the seminal examination was satisfactory.

December 29th, 1941. Patient now states that she has had considerable abdominal pain for some time.

February 25th, 1942. Laparotomy performed 6 weeks ago by a colleague. Chocolate cyst of left ovary found—proved by section. The patient had had 2 periods in February. On February 1st and 19th both breasts were secreting creamy milk in large quantities and were full and uncomfortable. She was given 5 mg. stilboestrol t.d.s. for 5 days.

March 5th, 1942. Breasts more comfortable but still secreting large quantities of watery milk—a stream 6 feet long could easily be obtained by pressure on them. Tubal patency again tested. Negative at 200 mm. Hg (13th day).

Comment. The combination of tubal occlusion and ovarian endometriosis will account for the sterility. I do not know what hormonal imbalance caused the extreme lacteal secretion in a nulliparous woman, and have not encountered a similar phenomenon before or since.

CASE No. 31. Yoruba tribe. Age 31. Married 2 years. Menarche aged 15. Cycle normal. Scanty loss. For 3 years has had dysmenorrhoea of a congestive type beginning the day before the period and lasting 3 days. Has had to go to bed with pain and fever. No dyspareunia. Complains of seminal efflux. History of gonorrhoea and white discharge for 3 years. Fourteen years ago had a 3 months' abortion and apparently another 2 months' abortion 3 months ago. Her husband has 3 children by another wife, the youngest aged 4.

On examination a tumour 4 inches in diameter could be felt in the right iliac fossa and in the right fornix, pushing the uterus over to the left.

November 9th, 1941. Right pyosalpinx drained. January 14th, 1942. Wound healed. Nothing abnormal could now be detected *per vaginam.*

Comment. A typical case of a large tubo-ovarian abscess.

CASE No. 32. Yoruba. Normal height and weight. Estimated age 30. Married 15 years. primary sterility. History of discharge 10 years, but not gonorrhoea. Marked frequency of micturition—about 8 times per hour. Husband has 2 children by another wife. *On examination.* Clitoris circumcised (very unusual in a Yoruba). Pin-hole os. Tender over bladder. Cervical smear—Moderate number of epithelial cells, very few pus cells, many mixed organisms, no gonococci. Catheter specimen of urine—many pus cells. No *schistosoma haemotobium.* Numerous gram negative intra- and extra-cellular diplococci. Given a week's treatment with sulphapyridine but, although much improved, the frequency was still present.

Comment. This case is recorded as the only case of gonococcal cystitis encountered.

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CASE No. 56. Estimated age 30. Married 11 years. Menstrual history normal. Libido good but intercourse only about twice a month, presumably because the husband has 8 other wives. Between them these wives have 6 children, youngest aged 1 year. The patient had 1 child 11 years ago but it died.

On examination the patient's physique is fair. The breasts are enlarged and pendulous. The vagina is very spacious and easily admits the whole hand although there is no prolapse of uterus or vaginal walls. Cervix thick, large and hard. Discharge excessive. Uterus retroverted, fixed and enlarged to the size of a 4 months' pregnancy. Small fibroids in anterior wall and a large one posteriorly. Adnexae adherent but not tender. Tubal patency positive on left side at 110 mm. Hg.

Cervical smear—pus cells very numerous, intra- and extra-cellular gonococci present.

Comment. In spite of the numerous positive pelvic findings the left Fallopian tube was still undoubtedly patent. The patient would not submit to operation after the gonorrhoea had been treated.

CASE No. 87. Yoruba. Height 5 feet. Weight 8 stones. Age 27. Secondary sterility. Two children aged 5 and 4. Married 4 years. Menarche unknown. Cycle 22 to 25 days. Loss 5 days. Scanty. Some dysmenorrhoea of congestive type. No dyspareunia. Libido good. Intercourse once a week. Husband has 1 other wife with 2 small children.

No history of gonorrhoea but vaginal discharge for last 10 months.

On examination. Good physique. Breasts lax. Male distribution of pubic hair. Moderate vaginal discharge. Cervix multiparous. Uterus retroverted but not fixed. No adnexal swelling.

December 24th, 1941. Cervical smear—a few pus cells, many mixed organisms, no gonococci.

Tubal patency negative at 120 mm. Hg. (10th day cycle). Treatment was commenced with intramuscular injections of sterilized suspension of sulphapyridine tablets, 1 g. daily for 6 days. (This treatment was used a great deal in West Africa as it was found to be very efficacious for cases of gonorrhoea and economical of a drug in short supply. The protein of the tablet or tissue necrosis produced a febrile reaction of 102 to 104°F. and although it invariably caused a massive brawny oedema at the site of the injection and was very painful, suppuration never occurred and the muscle returned to normal within a week.)

February 2nd, 1942. Tubal patency repeated. Positive at 90 mm. Hg. (18th day cycle).

Comment. This case shows that a combination of sulpha drugs and fever therapy may be responsible for successful treatment of non-patent Fallopian tubes. Several such apparent successes were obtained, although it must always be remembered that repeated insufflation alone may be sufficient to establish patency.

CASE No. 91. Yoruba. Estimated age 32. Married 17 years. Two children, aged 16 and 13. Menstrual history normal. No dyspareunia. Intercourse once a week. No history of discharge or gonorrhoea. Husband has 2 other wives. There is 1 child aged 3 months.

On examination the only abnormal finding was a thick infected cervix. Cervix cauterized on 2 occasions. Tubal patency tested on 2 occasions and found to be patent at 40 and 50 mm. Hg. (10th and 16th days). Endometrium shows secretory phase well marked on 23rd day of cycle.

Comment. This shows the rare case in which no definite cause of 13 years' sterility can be found, although even here the infected cervix may be responsible and the man may be subfertile, as although he has a child 3 months old, this is the only impregnation with 3 wives in many years.

CASE No. 94. Ibo tribe. Height, 5 feet. Weight, 8 stones. Primary sterility. Married 2 years 9 months. Menstrual loss excessive. Severe dysmenorrhoea for which she has sometimes to go to bed. No dyspareunia. Complains of seminal efflux. Intercourse twice a week. No history of discharge or gonorrhoea.

On examination. Physique good. Circumcised. Some discharge. Cervix very elongated and pinhole. Uterus and adnexae normal. Cervical smear—epithelial cells +, no pus or gonococci. The husband has no other wives. He has had " about 20 attacks of gonorrhoea."

On examination. Right testicle large. Well-marked epididymitis. Scars on penis left side and

enlarged inguinal glands. Has many other enlarged glands—neck, axilla, etc. Seminal examination—3 ml. opaque watery fluid. A few pus and epithelial cells. Azoospermia. Kahn test—positive.

Comment. An example of complete sterility in the male with little clinical evidence that there is much wrong with the wife.

CASE No. 98. Yoruba. Height, 5 feet 2 inches. Weight, 7½ stones. Age 31. Married 11 years. Secondary sterility. Menstrual history normal. One child in 1932. Two months' miscarriage in 1935. Discharge since childbirth in 1932.

On examination. Fair physique. Cervix scarred. Uterus retroverted. No adnexal swelling. Cervical smear—moderate number of pus cells, intra- and extra-cellular gonococci present. Tubal patency negative on 2 occasions (after treatment and cervical smear negative for gonococci). The husband has no other wives and stated he has never had gonorrhoea. On physical examination he was perfectly normal and the seminal examination was perfectly satisfactory.

Comment. A case in which the woman appears to be entirely responsible for the sterility. It is odd that the husband should not get gonorrhoea from a positive case, but there is usually no reluctance to admit the disease.

CASE No. 103. Pagan. Height 5 feet 2 inches. Weight, 8 stones. Estimated age 28. Married 10 years. Primary sterility. Menstrual cycle normal. Loss rather excessive. Moderate dysmenorrhoea. Has had dyspareunia for 1 year. No history of gonorrhoea or discharge. Husband has 1 other wife with 2 children, the youngest 1 month old.

On examination no abnormality noted except a pin-hole os. Kahn negative. Cervical smear—a few pus cells, no gonococci.

August 13th, 1942. Dilatation and curettage. Normal secretory-phase endometrium obtained (21st day of cycle). Stool, blood and urine examinations normal.

May 26th, 1945. Normal delivery of full-time child.

Comment. A case comparable to those so frequently seen in this country in which a dilatation and curettage was all that was required after 10 years of sterility. This is one of the few cases on which a follow-up was obtained. Africans are realists. For example one patient seen by chance in the antenatal clinic, when asked why she had not reported as requested, said "Why should I? I came complaining of sterility and there is no need for me to have any further treatment." Case 115 is similar.

CASE N. 105. A Baminda of the Cameroons. Height, 5 feet 8 inches. Weight, 9 stones. Estimated age 28. Secondary sterility. 1 child 8 years old and a 2 months' abortion 1 year ago. Menstrual cycle, normal. Two years moderate dysmenorrhoea and 1 year slight dyspareunia. History of gonorrhoea 5 years ago and a vaginal discharge since then. Pneumonia 1 year ago. Husband has 3 other wives with 4 children, and the youngest aged 3.

On examination. Physique good. Breasts lax. Cervix multiparous. On abdominal examination a mass arising out of the pelvis and reaching to the umbilicus could be felt. A depression in the midline suggests that this mass is divided into two halves. To the right there is some tenderness.

Per vaginum. This mass is almost immovable and the uterus could not be detected separately from it. Cervical smear—no pus cells or gonococci.

August 2nd, 1942. Exploratory laparotomy. Bilateral ovarian cysts firmly adherent to small bowel, rectum and pelvic wall. Left cyst removed, leaving some of the posterior wall of the cyst. Right partially removed. Two locules contained old blood. Large, rightsided pyosalpinx entered and drained.

August 19th, 1942. Good progress. Tube out and no abdominal mass felt now. White blood count 15,300; 65 per cent polymorphonuclears. Kahn test—positive. Bowel—ova of ascaris, ankylostomes and trichuria present. Urine—pus cells and red blood cells present. No *schistosoma haematobium*. This patient was again seen by a colleague on April 7th, 1943. She had then a profuse vaginal discharge. Cervical smear contained numerous pus cells and was positive for gonococci. The pelvis was almost clear on

vaginal examination. Given treatment for this fresh infection of gonorrhoea.

Comment. An example of a not unusual type of pelvis found at laparotomy in Africans. Note the numerous other pathological findings.

CASE No. 117. Yoruba tribe. Height, 5 feet 2 inches. Weight, 7 stone. Age estimated at 25. Married 10 years. Primary sterility. Menstrual cycle normal. Loss excessive and always very severe premenstrual and menstrual dysmenorrhoea. Slight dyspareunia for 7 years. Husband has 1 other wife with 2 children, the youngest aged 1 year. No history of gonorrhoea, but some discharge.

On examination. Physique poor. Breasts small. Cervix—small erosion. Slight discharge. The uterus seemed to be about the size of a 3 months' pregnancy. Last menstrual period 3 weeks ago. Uterus not tender and no swelling felt in fornices separate from uterus. Cervical smear—no pus cells, no gonococci. Ide—Negative.

September 11th, 1942. Laparotomy. Many adhesions. Swelling found to be enlarged right ovary containing pus and firmly adherent to back of uterus. The right Fallopian tube was inflamed and bound down by adhesions. This and the right ovary were removed. Adhesions in the region of the left fimbria were broken down and the left Fallopian tube made patent to silkworm gut.

October 26th, 1942. Tubal patency negative at 180 mm. Hg. (13th day of cycle).

February 8th, 1943. Tubal patency negative 6th day.

Comment. Another typical case of pelvic inflammatory disease, the diagnosis being in error pre-operatively. Also illustrates the difficulty of maintaining the re-establishment of tubal patency after operative procedures.

CASE No. 132. A tall thin woman, estimated age 35. Falani tribe. Primary sterility. Married 11 years. Menstrual cycle regular until 1 year ago. Since then has been 3 months without periods on 3 occasions. No dysmenorrhoea. Severe dyspareunia for 6 years. No history of gonorrhoea but discharge excessive for 7 years. The husband has no other wives and would not appear for examination.

On examination. Poor physique. Breasts, pubic hair, pelvis—normal female type. Not circumcised. Vaginal atresia almost complete 3 inches from the introitus. Cervix not felt. No gross abnormality in pelvis. This patient was asked to return for a plastic vaginal operation but failed to return.

Comment. Vaginal atresia is not an uncommon condition in African women, and is of a different type from the congenital variety seen occasionally in this country. There is no hard fibrous or cartilaginous ring felt at the point of stricture. The most likely explanation, which might or might not fit in with this particular case, is that the woman acquired a gonococcal vaginitis before or near puberty and the resulting inflammation led to vaginal atresia. In 1 case this condition was seen in a woman at full time in labour. It was with the utmost difficulty that a minute opening was found with a probe in the vaginal vault. On stretching this with the finger the vaginal wall started to tear and a Caesarean section had to be performed.

CASE No. 134. Hausa tribe. Secondary sterility. One child aged 8. The labour was apparently normal. One year later the uterus prolapsed outside the vulva and has remained there ever since. Husband has 1 other wife and no other children.

On examination. Fair physique. Breasts lax and small. Abdominal muscles good. No abnormality felt on palpation. There is complete uterine prolapse and an ulcer 1 inch in diameter over the cervix. Ide—positive.

September 7th, 1942. Ulcer treated daily with flavine dressings. September 18th. Ulcer healed. Fothergill's operation performed. October 10th, Very satisfactory result.

Comment. Prolapse of all types is extremely rare in African women, and the only 2 cases I saw which required any treatment were complete procidentias. This is probably due to their fine muscular development, the hard work the women have to do

and the fact that they are on their feet in a matter of hours after delivery.

CASE No. 138. Falani tribe. Primary sterility. Married 6 years (2 with present husband). Menstrual cycle normal. For 2 months severe abdominal pains and vaginal discharge. Admitted that she had probably acquired an infection from another man. Husband has 2 other wives but no children. Menstrual history normal.

On examination practically no breast development at all. Ulcer on fourchette. Foul profuse vaginal discharge. Thickening and oedema of vagina, especially posterior wall and extending on to rectum. Glands palpable in both inguinal regions. Cervix feels hard and craggy. Ide—negative. *Schistoma haematobium* in urine. Cervical smear—no gonococci, spirochetes + +. This patient was given a course of intramuscular sulphonamide with considerable alleviation of the vaginal discharge, but the vaginal and rectal thickening remained. She was also treated with stovarsol locally and the ulcer and spirochetes disappeared.

Comment. This case illustrates 2 conditions—both of which are quite common in Africans.

1. Lymphogranuloma inguinale. Stammers and Law (1942) wrote an article on lymphogranuloma inguinale in Africans in Sierra Leone. They apparently obtained excellent results in the treatment of this disease with sulphonamide. In Nigeria the results were very poor and many of us considered that if the condition cleared up with sulphonamides it was a soft sore with which we were dealing. If it did not make any difference we diagnosed lymphogranuloma inguinale with confidence.

2. Spirochaetal infection of the lower genital tract. Several of these cases were seen. They responded well to arsenic and the condition appeared to be analagous to Vincent's angina.

CASE No. 143. Ibo tribe. Aged 17. Married 2 years. Primary sterility. Menstrual cycle normal. Moderate premenstrual dysmenorrhoea

for 1 week and during menstruation since puberty, which occurred when she was 14. No dyspareunia. Husband has no other wives and would not come for interview.

October 8th, 1942. *On examination* Small woman of fair physique. Breasts undeveloped. Pubic hair and fat distribution—male tendencies. Circumcised. Moderate discharge. Cervix normal. Uterus rather bulky and tender, thickening in left fornix. Cervical smear—no pus cells or gonococci. April 29th, 1943. Examined in maternity clinic— 4 months' pregnant.

Comment. Although very incompletely investigated this case is of interest in that in spite of a tender palpable tumour in the left fornix she became pregnant within 2 months. This bears out the previous observation made that a palpable inflammatory mass on one side does not exclude tubal patency on the other.

CASE No. 169. Effik of Calibar. Height, 5 feet 3 inches. Weight, 8 stones. Primary sterility. Estimated age 20. Married 2 years. Menstrual cycle normal. Severe menstrual dysmenorrhoea of congestive type always. Three years ago was in bed for 6 months with severe right-sided abdominal pain.

January 2nd, 1943. Brought into hospital with severe right-sided pain, 3 days anuria and constipation.

On examination. Pubic hair of male distribution. Large abdominal swelling extending from right iliac fossa to the pouch of Douglas. Very tender. Uterus could not be felt because of pain. Treated with hot fomentations and sulphonamides.

January 20th, 1942. Large tubo-ovarian abscess drained abdominally. February 2nd. Tube out. Excellent progress. Slight thickening only felt *per vaginam.*

Comment. One of the very few cases of tubo-ovarian abscess I have seen in a West African with acute symptoms. Although it has not been stressed in her history, one of her chief complaints, even on admission, was sterility.

CASE No. 175. Effik. Estimated age 25. Married 4 years. Primary sterility. Menstrual cycle normal

until 1 year ago, since when she has had secondary amenorrhoea. Always severe dysmenorrhoea. No dyspareunia. Intercourse twice per month. Husband has no other wives.

On examination. Good physique. Mucous membranes very pale. Body fat and pubic hair shows male tendencies. Circumcised. Vagina small. Cervix small. Uterus small and retroverted. Nil in fornices. No discharge. Haemoglobin 35 per cent. Colour index 0.7. Endometrium—absent. Cause of anaemia not found. The patient was given full doses of iron and liver.

June 3rd, 1943. (Colleague's notes.) Three months pregnant.

Comment. A case of severe hypochromic anaemia who responded to treatment and became pregnant.

CASES NOS. 194 AND 195. These are taken together as they are the wives of the same husband.

	194	195
Tribe	Yoruba	Yoruba
Age (estimated)	28	20
Married	12 years	8 years
Menstrual cycle	Normal	Normal
Dysmenorrhoea	8 days premenstrual, of congestive type	4 years menstrual—griping
Dyspareunia	No	No
Children	1, 7 years old	1, 4 years old
Discharge	For 2 years	Since birth of child 4 years ago
Examination		
Physique	Good	Good
Breasts	Lax	Normal
Pubic hair	Tendency to male	Tendency to male
Vagina	Large, lax, slight cystocele	Normal
Cervix	Large erosion Thick pus Bleeds easily	Small erosion Bleeds easily
Uterus	Bulky Tender	Pulled over to left. Deep in pelvis.
Adnexa	Nil	Nil
Tubal patency	Not done	Negative at 180 mm. Hg.

Cervical smear Not taken   Moderate number pus cells. No gonococci.

The husband of these 2 cases gave a history of gonorrhoea on 11 different occasions. Seminal examination—283,000 spermatozoa per ml. Motile. A few pus cells.

Comment. There is little doubt that both wives have been sterilized by gonorrhoea after having children. The husband's fertilizing powers appear to be unaffected after 11 infections of gonorrhoea.

SUMMARY.

1. A brief historical survey of sterility is given.

2. Introduction: 203 cases of sterility in West Africans have been investigated. The amenities and restrictions of the investigation are considered. The customs of the natives and the local conditions relevant to the subject are discussed. Differences between European and African modes of life and conduct are considered.

Although tropical diseases may play a considerable part in regard to sterility in the West African, reasons are given why these factors are not considered in this paper.

3. An analysis of the material obtained is presented, each contributing factor of sterility being treated separately. A comparison is made between these findings and the published reports on the subjects.

The following facts emerge:

(a) Genital sepsis, for which undoubtedly gonorrhoea is largely responsible, is the major cause of sterility in West Africans. This is due to the prevalence of the disease, but there is evidence to show that each separate infection of gonorrhoea in the West African is less severe than in the European and is less likely to cause permanent damage.

The virtual absence of puerperal and postabortal fever is noted, and reasons given.

(b) The prevalent belief that the menarche in Africans starts early in life is questioned. Female genital maldevelopment and immaturity are found to be more common than in European women. Case histories to illustrate this are given.

(c) Anovulatory menstruation, endometriosis and tuberculous endometritis occurring in the West African women are compared with the findings in the literature. No conclusive differences are found, but the material obtained for a comparison of these subjects is small.

(d) Abortions are found to occur as frequently as in the white races. Habitual aborters are fairly common among West African women. Case histories of these are given. The difficulty of assessing the significance of syphilis in cases of abortion is explained. There is some evidence to show that it may be of considerable importance.

(e) Uterine myomata are found to be no more common than in the white races. This finding conflicts with the literature on American negroes, in whom all writers find a marked preponderance of this disease. The American negro comes from the same stock as the West African negro, but no explanation of this finding is obvious.

(f) The virtual absence of psychological factors, which play such an important part in cases of sterility in Europe and America, is considered and reasons for this difference given.

(g) The male responsibility in cases of sterility in the West African is surveyed. This again demonstrates the importance of gonorrhoea. The polygamous habits of the West African give data of considerable value as regards biological fertility. A limited comparison of biological and laboratory fertility is able to be made. An incidence of ·38.5 per cent of male sterility or marked subfertility is found.

4. A selection of typical case-histories is presented, as it is felt that these give a truer picture of the whole aspect of the problem. Comments on each case are appended.

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Calcium and Phosphorus Metabolism in Pregnancy
(A Survey under War and Post-War Conditions)

IV. Calcium and Phosphorus Balances and Antenatal Findings

BY

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In previous papers (Obermer, 1946a, 1946b, 1947) tables have been given showing the calcium intake and output figures of 48 healthy out-patient gravidae (40 primiparae and 8 cases of second pregnancy) who were investigated at roughly 6-weekly intervals throughout pregnancy. These cases were divided into 4 groups: Group I controls; Group II with a supplement of calcium phosphate in 2 different forms; Group III with a supplement of two forms of calcium phosphate together with large doses of Calciferol, and Group IV with varying doses of Calciferol only. The purpose of this preliminary grouping was to contrast the findings on a low calcium and phosphorus intake, with and without the addition of Calciferol, with those of a high calcium and phosphorus intake, also with and without Calciferol. Using the figures grouped in this way certain tentative conclusions were drawn (Obermer, 1947).

In attempting to correlate the antenatal and, later, labour and postnatal findings with the biochemical findings (confined, in this paper, to the calcium and phosphorus balances) it may, however, be useful to extend the grouping, taking 2 further factors into consideration:

(a) That Groups II and III cases were given different forms of calcium phosphate. One half were given so-called "colloidol" calcium phosphate made from bone, in the form of "Calfos" tablets, the other half tablets of ordinary calcium phosphate B.P.

(b) That there was a wide range of Calciferol dosage in Group IV. Doses of over 10,000 I.U. per day seemed to exert a definite, though inconstant, effect on calcium and phosphorus metabolism. With smaller doses the findings were inconclusive.

In this paper, therefore, it is proposed to divide the findings into the following groups:

Group A. Controls.

Group B. Supplement of "Calfos" tablets.

Group C. Supplement of "Calfos" tablets together with large doses of Calciferol.

Group D. Supplement of calcium phosphate B.P. tablets.

Group E. Supplement of calcium phosphate tablets together with Calciferol.[†]

Group F. Supplement of Calciferol only, in varying doses—from 800 to 10,000 I.U.

Group G. Supplement of Calciferol only, in varying doses—from 10,000 to 36,000 I.U. per 24 hours.

Doses per 24 Hours.

*Groups B, C, D, and E	Calcium	Phosphorus
3rd to 5th months	0 64 g.	0.282 g.
6th to 7th months	0 95 g	0.423 g.
8th month to term	1 26 g	0.564 g.

†Groups C, and E	Calciferol
3rd to 5th months	18,000 I U.
6th to 7th months	27,000 I.U.
8th month to term	36,000 I.U.

The net plus or minus balances of both calcium and phosphorus, for each case in each group, have been added up and divided by the number of 48-hour investigations. A mean 48-hour balance has thus been arrived at for each group. In Table I the mean 48-hour figure has been further divided by 2 to give the mean 24-hour balance.

of a percentage of the total maternal reserves. For calcium, at any rate, such a figure can be arrived at with relative accuracy, as the skeleton contains 99 per cent of the calcium in the body of the mother. In the case of phosphorus, the percentage is lower—just over 90 per cent. In Table II, however, there is a maternal loss of phosphorus in only 2 out of the 7

TABLE I.

Mean 24-hour Calcium and Phosphorus Balances of Each Group of Cases.
(Expressed in Grammes)

Group	Number of cases	Number of 48-hour investigations	Mean daily calcium balance	Mean daily phosphorus balance
A	6	27	−0.48	+0.10
B	6	29	−0.08	+0.15
C	7	33	+0.06	+0.32
D	6	26	+0.004	−0.04
E	6	31	−0.004	+0.13
F	10	42	−0.32	−0.002
G	7	38	−0.16	+0.06

It has been necessary to assume that the five or six 48-hour investigations carried out, during the pregnancy of each case, were representative of the whole period. Such an assumption is legitimate only for purposes of comparison and discussion. Longer and more frequent balance periods would be necessary for the figures to be considered conclusive. Certain tendencies, do, however, emerge. Their basic significance to the maternal organism is made clearer by calculating the total maternal loss or gain throughout pregnancy as in Table II.

In the first and fourth columns the figures are arrived at by multiplying the mean daily calcium and phosphorus balances by 280. The foetal requirement figures, in the second and fourth columns, represent a compromise between the figures calculated by Mitchell and Curzon (1939) and those given by Shohl (1939).

The net loss can be expressed in terms

groups. No attempt, therefore, will be made to present the phosphorus figures in percentage of maternal reserves. On the other hand there is a maternal loss of calcium in all 7 groups. In the discussion which follows, this calcium loss will be converted into a percentage of the maternal reserves, by accepting Shohl's figure of 1,150 g. as the calcium content of the skeleton of an adult male weighing 66.2 kg. Making a small allowance (5 per cent) for sex-difference in size of bones, this figure will be corrected for the mean weight of each group. For instance, in Group A the mean weight was 56 kg. The calcium skeletal reserve in this group is calculated, therefore to be 975 g.

Groups A, F, and G, will be considered first, as the calcium intake in these groups was equally low, whilst the calcium intake in Groups B, C, D, and E, was high, owing to the generous supplements.

Group A. The maternal loss of 165 g.

TABLE II.

Total Maternal Loss or Gain of Calcium and Phosphorus, throughout Pregnancy, of Each Group. (Expressed in grammes)

Group	Calcium			Phosphorus		
	Balance throughout pregnancy	Content of foetus	Total maternal loss or gain	Balance throughout pregnancy	Content of foetus	Total maternal loss or gain
A	− 135	25	− 160	+ 28	14	+ 14
B	− 20	25	− 45	+ 42	14	+ 28
C	+ 17	25	− 8	+ 90	14	+ 76
D	− 1	25	− 24	− 11	14	− 25
E	− 1	25	− 26	+ 36	14	+ 22
F	− 90	25	− 115	− 0.5	14	− 14.5
G	− 45	25	− 70	+ 17	14	+ 3

represents 16 per cent of the total calcium reserve in the body.

Group F. As the mean weight of this group was 62 kg. the maternal loss of 115 g. represents 11 per cent of the total calcium reserves. Such a diminution, as compared with A, is not statistically significant. Further, there is a slight phosphorus loss as compared with a slight phosphorus gain in Group A. Thus these figures do not provide evidence that doses of Calciferol smaller than 10,000 I.U. per day exert a definite influence on calcium and phosphorus metabolism during pregnancy —when the calcium intake is suboptimal.

Group G. With a mean weight of 60 kg. a maternal loss of 70 g. represents 7 per cent of the calcium reserves. As there is a slight phosphorus gain in this group, a reduction from 16 per cent (control Group A) to 7 per cent may be considered suggestive, if not conclusive. Hence it is probable that doses larger than 10,000 I.U. per day exert some influence on calcium and phosphorus metabolism, even on a sub-optimal intake of calcium.

Group B. With a mean weight of 60 kg. the maternal loss of 45 g. represents 5 per cent of the maternal reserves. There is also a definite phosphorus gain.

Group C. With a mean weight of 56 kg. the small maternal loss of 8 g. represents less than 1 per cent of the maternal reserves. There is also a gain of 76 g. of phosphorus —much higher than in any other group. This is the only group in which the balance figures nearly reach a theoretically desirable standard. It is probable, therefore, that large doses of Calciferol, together with adequate supplements of an assimilable form of calcium phosphate, are the best way of ensuring calcium and phosphorus retention—in the average pregnant woman on a mixed diet.

Group D. With a mean weight of 54 kg. the loss of 24 g. represents only 2.6 per cent of the maternal reserves. On the other hand, the phosphorus loss is 10 g. over and above the foetal requirements.

Group E. With a mean weight of 50 kg. the calcium loss of 26 g. represents 3.2 per cent of the maternal reserves. This figure is not materially different from the percentage loss in Group D. A definite phosphorus loss in the latter group, however, has been converted into a definite phosphorus gain. As Groups D and E were given the same supplement of calcium phosphate B.P., the figures in these 2 groups suggest (a) that calcium phosphate B.P. may be less assimilable than "Calfos" and (b) that the Calciferol effect is exerted more directly upon phosphorus than upon calcium metabolism.

ANTENATAL FINDINGS.

As well as the 48 cases dealt with above, 6 further cases were investigated, on one occasion only, during the early part of pregnancy.

The total calcium intake and output figures of these cases have been given in Table I of a previous paper (Obermer, 1946a) (cases 7 to 12). These cases were, of course, not given any supplements of calcium and phosphorus. Their calcium and phosphorus balances are given in Table III.

As the overwhelming majority of the control cases (Group A) and the pre-supplement investigations of the other groups had negative calcium balances, it is reasonable to assume that cases 34, 37 and 44 had similar negative balances to cases 7 and 8 —see Table III. Thus 5 primiparae out of 45, i.e., 11 per cent, had a negative calcium balances (2 definite and 3 presumed) and also had spontaneous miscarriages As this is, probably, a somewhat higher percentage than normal pregnant women, it suggests that a negative calcium balance may

TABLE III.
48-hour Calcium and Phosphorus Balances of Cases Investigated Once Only in the Early Part of Pregnancy. (Expressed in grammes)

Case No.	Date	Week	Calcium balance	Phosphorus balance
7	25.10.1943	9	−0.51	+0.36
8	24. 4.1944	9	−0.93	−0.37
9	19. 5.1944	12	−0.61	−0.16
10	4. 5.1943	20	−0.15	+1.05
11	4.10.1944	9	−0.14	+0.56
12	30. 9.1944	10	−2.17	−0.24

Cases 9, 11 and 12 were evacuated from London and were lost sight of.

Case 10 developed pyelitis of pregnancy, went into hospital and could not be investigated any further.

Case 7 had a spontaneous miscarriage at the 13th week.

Case 8 had a spontaneous miscarriage at the 12th week.

Miscarriages.

Of the 54 cases whose balances have been given above, 45 were primiparae.

In the 40 out of these 45 primiparae who were investigated throughout pregnancy, during the present survey, there were no miscarriages. Three cases out of the 40, however, had previously had spontaneous miscarriages—cases 34 (Obermer, 1946b), 37 and 44 (Obermer, 1947) (cases 37 and 44 one each at 3 months and case 44 two at 3 months).

be one of a large number of factors which predispose towards spontaneous abortion.

It is equally obvious that a negative calcium balance, with or without a negative phosphorus balance, does not necessarily imply the inevitability or even the probability of spontaneous abortion.

The balance figures for cases 34, 37 and 44, during the present survey, are given in Table IV.

On this occasion each of these 3 cases had a normal pregnancy and labour. Though cases 34 and 37 show positive balances of both calcium and phosphorus, case 44 showed a heavy negative balance of both elements.

Intrauterine Death.

Of the 48 cases investigated throughout pregnancy 8 were cases of a second pregnancy. In 6 out of the 8 cases previous

TABLE IV.

Mean Daily Calcium and Phosphorus Balance Figures of Three Cases Referring to Discussion on Miscarriage.

Case No.	Group	No. of investigations	Mean daily calcium balance (g.)	Mean daily phosphorus balance (g.)
34	E	5	+0.35	+0.56
37	F	4	+0.25	+0.60
44	F	4	−0.65	−0.38

pregnancy had been normal and resulted in normal labour and a healthy child.

Two cases had been abnormal during the previous pregnancy. Number 13 had suffered from severe toxaemia of pregnancy, which had been terminated by surgical induction at the 32nd week, resulting in a stillborn foetus weighing 2 pounds 14 ounces.

Case 43 had also suffered from toxaemia in her previous pregnancy, which had been allowed to continue. She was delivered of a 6-weeks premature baby, which died of convulsions after 27 hours.

Both these patients had a successful second pregnancy. Case 43 had an un-foetus died *in utero* somewhere between the 31st and 37th weeks. Labour was induced at the 38th week and resulted in a dead foetus of 5 pounds 10 ounces.

The balance figures for these 3 cases are given in Table V.

Though case 3, whose foetus died *in utero*, had both negative calcium and phosphorus balances throughout pregnancy, cases 13 and 43, whose babies survived on this occasion, also showed negative calcium balances. Their phosphorus balances were positive.

It is probable that a disturbance of calcium and phosphorus metabolism may, directly or indirectly, play some part in the

TABLE V.

Mean Daily Calcium and Phosphorus Balance Figures Referring to Discussion on Foetal Intra-uterine Death.

Case No.	Group	No. of investigations	Mean daily calcium balance (g.)	Mean daily phosphorus balance (g.)
13	B	5	−0.58	+0.015
43	F	5	−0.31	+0.16
3	A	5	−0.41	−0.16

eventful pregnancy, throughout the period of investigation, a normal labour and a healthy child. Case 13 had a slight rise of arterial pressure at the 30th week, which subsided on rest and diet, but she also had a normal labour and a healthy child.

Case 3, in the Control or A Group, was the only one of this series whose pregnancy did not continue successfully to term. The mechanism of toxaemia, intrauterine death and unsuccessful nidation. So many factors are involved in these phenomena, however, that it is impossible to assess the importance of any part thus played.

The fact that 3 women, who had previously aborted and 2 women, in whom previous intrauterine foetal death had occurred, went successfully to term, when

given supplements of calcium phosphate and / or Calciferol, may have nothing to do with these supplements. The element of chance cannot be excluded. Further, the fact that all these cases were singled out for special investigation and treatment may have given them a feeling of security. We do not yet know the physiological effects of the latter, but its importance should not be underestimated. We need the findings of a much larger series than the present one before we can hope to determine the quantitative importance of calcium and phosphorus retention during pregnancy, in these circumstances.

Symptoms During Pregnancy.

In only 2 cases out of the 48 (apart from the intrauterine death in case 3) were there any disturbing symptoms or signs during pregnancy. One case (13) has already been discussed. In another case (39) there was also a rise of arterial pressure in the 26th week, though there were no abnormal symptoms. She was, therefore, made to rest from the 23rd week to the 32nd week at home, and from the 33rd week to the 40th week at Brocket Hall. For 2 weeks of this period she was on a low protein diet.

The mean daily balance figures of this case were:

Case No. 39; Group F.
Number of investigations 4
Mean 24-hour calcium balance .. ... − 0.28
Mean 24-hour phosphorus balance .. ... − 0.12

The remaining 45 cases of this series had normal pregnancies. Careful note was taken of minor symptoms. As would be expected, however, no correlation could be found between these symptoms and the calcium and phosphorus balance figures.

In Table VI the cases were classified according to the following criteria :

Nil. No nausea or vomiting. No other symptoms throughout.

Very slight. Nausea only up to the third month. No other symptoms.

TABLE VI.
Symptoms of Pregnancy.
(Total number of cases 48)

Nil.					
Number of cases	...	...	...	...	14
Percentage of total	...	...	...	...	29
Very slight.					
Number of cases	...	...	...	...	19
Percentage of total	...	...	...	...	39.5
Slight.					
Number of cases	...	...	...	...	13
Percentage of total	...	...	...	...	27
More than slight.					
Number of cases	...	...	...	...	2
Percentage of total	...	...	...	...	4.5

Slight. Nausea accompanied by actual vomiting and, in some instances, prolonged beyond the third month. Also digestive symptoms, neuritis and other minor disturbances.

More than slight. Symptoms or signs calling for rest in bed, dietetic treatment or other active intervention.

TABLE VII.
General Well-being Throughout Pregnancy.
(Total number of cases 48)

No change.					
Number of cases ...	...	...	...	...	27
Percentage of total	...	...	...	...	56
Increase.					
Number of cases ...	...	...	...	...	8
Percentage of total	..	...	...	...	17
Decrease.					
Number of cases ...	...	...	...	...	13
Percentage of total	...	...	...	...	27

The fact that 73 per cent of these cases experienced no diminution in well-being and 17 per cent an actual increase in well-being is, perhaps, surprising in view of bombing and the many discomforts inseparable from wartime and the immediate post-war period.

SUMMARY.

1. The mean daily calcium and phosphorus balances of 48 healthy pregnant

women are given in tabular form. The figures are divided into 7 groups. A, Controls; B, Supplement of so-called "colloidal" calcium phosphate in the form of "Calfos" tablets. C, Supplement of "Calfos" tablets together with large doses of Calciferol. D, Supplement of calcium phosphate B.P. tablets. E, Supplement of calcium phosphate tablets together with Calciferol. F, Supplement of Calciferol only, in varying doses—from 800 to 10,000 I.U. G, Supplement of Calciferol only, in varying doses—from 10,000 to 36,000 I.U. per 24 hours.

2. From this table a calculation is made of the total material loss or gain of calcium and phosphorus throughout pregnancy.

3. The significance of the above figures is discussed and a further calculation is made showing the considerable degree of depletion of the maternal skeletal stores of calcium in Groups A and F.

Figures for Group G indicate that daily doses of Calciferol above 10,000 I.U. per day probably have some influence on calcium and phosphorus metabolism.

The figures from Groups B, C, D and E confirm the primary importance of a high calcium and phosphorus intake.

The findings for Groups B and C, as compared with D and E, suggest that calcium phosphate in a "natural" form may be assimilated more completely than ordinary calcium phosphate B.P.

4. The calcium and phosphorus balance figures are given for 6 further cases who were investigated, once only, during the early part of pregnancy. Four of these cases were lost sight of, 2 had spontaneous abortions at the third month.

Calcium and phosphorus balance figures are also given for 3 cases (out of the 48) who had previously aborted (spontaneously) but who successfully carried through to term in the present survey.

The possibility is discussed of phosphorus and calcium retention playing some part, among many other factors, in the successful nidation of the ovum.

5. Calcium and phosphorus balance figures are given for 3 further cases of second pregnancy. In 2 of these cases there had been severe toxaemia during the first pregnancy. Foetal death *in utero* had occurred in one and neonatal foetal death in the second. In the third case intrauterine death of the foetus occurred at about the 32nd week of the second pregnancy—during the present survey. This third case belonged to the Control or A Group and showed heavy maternal loss of calcium and phosphorus.

6. Other variables are discussed which which may have been responsible for the successful conclusion of pregnancy and labour in the supplemented cases of this series who had previously aborted or suffered intrauterine or neonatal foetal death.

Stress is laid on the possible importance of emotional factors, in particular a sense of security due to the special interest shown, the special investigations and treatment.

7. Tables of the incidence of minor symptoms of pregnancy are given for the whole series. No correlation could be found between them and the calcium and phosphorus balances.

Details are given, in tabular form, as a contribution to the statistical study of normal pregnancy.

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Vestibular Anus
(Report of a Case)
BY

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ECTOPIC position of the anus in women is not uncommon and there are many reported cases in the literature, although few have been recorded in recent years. The majority of cases are noted in infants, · or in association with a pregnancy. This case is unusual in that the patient was aged 53, had had one confinement, and yet the abnormality remained unnoticed until she reported as an out-patient for an entirely different condition.

The cause of the condition is a failure in the development of the urogenital septum, which fails completely to separate the primitive cloaca into the sinus urogenitalis and the rectum. As a result, the cloacal duct persists, and the rectum may open anywhere on the posterior vaginal wall, vestibule or perineum. Other cases are noted where the rectum opens into either bladder or urethra.

Packard and Kirshbaum (1932) report a case in a primipara of 28 years of age, where Caesarean section was done to preserve the rectum intact.

Potts (1932) records a patient who had spontaneous vaginal delivery with an episiotomy. In a series of 8 cases he failed to note any complication of labour in 4 (2 were delivered by Caesarean section and in 2 more the result was unrecorded). If control is normal he suggests that operative measures to correct the deformity are inadvisable.

On the other hand, Cave (1937) has a successful case in a girl of 8, on whom he operated for faecal incontinence since infancy. He states the optimum time for operation is between the ages of 8 and 12 years. He gives the frequency as being between 1/10,000-1/70,000, as estimated by various authors.

David (1937) reports 6 cases in children and describes the operative technique used on 2 of them. He again stresses the point that operative treatment is undesirable if anal control is satisfactory.

Hipsley (1925) records a case where Caesarean section was performed in a primipara, partly for non-fixation of the head after several hours in labour, but mainly to avoid any damage to the levator muscles with possible loss of control. The patient stated she had control, provided the bowels were not loose.

Thompson (1894) records a girl of 19 years treated successfully by surgery.

Brenner (1915) discusses congenital defects of the anus and rectum. He records 10 cases of vulval anus in children, noted from birth up to 14 years of age. Immediate treatment is · directed to the relief of any obstructive symptoms. Six children were left for better development to occur, while 4 were operated on with good control resulting in all cases.

Johnston (1946) records the delivery of a primipara with this condition. Forceps delivery and episiotomy were required, the

PLATE I.   Vestibular Anus.

J.L.W.

child weighed 9 pounds 13 ounces and the rectovaginal septum was undamaged.

CASE REPORT. Mrs. A. T., age 53, was first seen at the out-patient department complaining of irregular discharge and bleeding *per vaginam* which on examination was found to be due to a carcinoma cervicis. The unusual condition of her anus was also noted, and during her treatment for the cervical lesion, an opportunity was taken to examine it more closely (Plate I).

The anal orifice was completely within the area of the vulva, being encircled posteriorly by the fourchette. The rectal mucosa protruded in cauliflower fashion, and no sphincter ani muscle could be detected. The recto-vaginal septum, easily palpated with one finger in the rectum and another in the vagina, was about ¼ inch thick.

The perineum showed no dimple or depression, which is sometimes present to mark the site of the anus, and measured 9 cm. from the fourchette to the tip of the coccyx.

The patient stated that as a child she had attended her doctor because of " something wrong with her back passage." Before marriage she again saw a doctor, who assured her the condition was no bar to matrimony.

Married in 1921, she had a normal delivery of a 7½ pounds child in 1931, after a labour of 20 hours. No perineal sutures were required.

Her sole disability appears to have been that if she took fruit or laxatives she became unable to control defaecation. Normally control of faeces and flatus is perfect.

DISCUSSION.

Abnormalities of this nature are usually noted at birth or during childhood. If overlooked at this time, they are usually observed during the course of a pregnancy.

Operative treatment is indicated only if symptoms of obstruction or incontinence are present. If control of defaecation is normal, most authorities agree that operative treatment is unwise.

When the condition is complicated by pregnancy, it makes an interesting obstetrical problem. Authorities differ as to whether Caesarean section should be performed, or normal vaginal delivery permitted. Certainly recorded cases who have had vaginal delivery do not appear to have suffered any subsequent loss of control. On the other hand, Caesarean section would certainly appear permissible to avoid any possibility of damage and laceration to the levator muscles and rectum.

SUMMARY.

1. A case of vestibular anus is described and some of the literature briefly summarized.

2. The majority of cases have good anal control and do not require operative treatment.

3. Caesarean section appears to have a place in the treatment if pregnancy ensues.

My thanks are due to Mr. Clifford White, under whose care this patient was admitted, for permission to publish this case.

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Cramps in Pregnancy

BY

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CALCIUM lactate has been for many years prescribed for the cramps from which pregnant women suffer. The results of this treatment have not been entirely successful. Several preparations of calcium have been used, with no better results than those obtained with calcium lactate. Some textbooks suggest pressure as a cause of these cramps, but Browne (1946) disagrees with this, and believes that the cause of the cramps is not fully understood. The idea underlying treatment with calcium lactate, seems to be that of a possible parathyroid deficiency. Richter, Holt and Barelare (1938), for example, administered large amounts of a solution of calcium lactate by mouth to parathyroidectomised rats, and found that in every case the symptoms of tetany disappeared. No signs of tetany are present in pregnant women who complain of cramp and the cramps do not disappear in every case following the administration of calcium lactate by mouth.

Glover (1931) found that heat cramps in industry were removed by the ingestion of extra sodium chloride. Marriott (1947) has listed cramps as one of the signs of salt-deficiency. Richter and Barelare (1938) carried out experiments which showed that in pregnant rats the appetite for calcium lactate increased, but not to anything like the same extent as their appetite for sodium chloride. They found that their appetite for calcium lactate increased in the first two-thirds of pregnancy and then fell

back to the normal level in the last third of pregnancy. It is in this last third of pregnancy in women that cramps are most troublesome. They also found that in pregnant rats the appetite for sodium chloride began to rise early in the first third of pregnancy and that it continued to rise right up to the end of the pregnancy. The total increase above the normal level in the appetite for calcium lactate was 50 per cent and for sodium chloride 300 per cent. Harding and Van Wyck (1926) found that the sodium chloride level in the blood of pregnant women rose steadily up to the 36th week and then very slowly began to fall. Most of the spontaneous recoveries from cramp in the untreated cases in the present investigation took place between the 36th and the 38th week of pregnancy.

It is not known what part this increased salt-intake plays. The fact that a similar rise in salt-appetite appears after adrenalectomy (Richter, 1936) suggests that the adrenal gland may play an important part in pregnancy. It is known that the adrenal gland enlarges in pregnant women (Dieckmann, 1942). Thorn and Harrop (1937) have shown that a close relationship exists between salt-metabolism and ovarian function.

During an investigation of the part played by hormones in failing lactation, Professor F. G. Young suggested to the investigator that these cramps in pregnancy might be a possible sign of adrenal insufficiency. This idea was based on the work of Richter which is mentioned above. The present investigation was started, there-

fore, under the auspices of the Medical Research Council at St. Thomas's Hospital in February 1945, and ended in September 1946. It began as an attempt to remove any sign of adrenal insufficiency during pregnancy in the hope that this might prevent failure of subsequent lactation.

DEFINITION OF CRAMP.

Cramp is a painful spasmodic contraction of the muscles of the limbs. During the paroxysm the muscular fibres affected can be felt gathered up into a hard knot. In pregnancy these cramps begin as early as the 20th week or as late as the 36th week. The commonest date of onset is the 28th week. They occur usually during the night but in severe cases may occur during the day as well. In the mildest cases stiffness is the only complaint. This stiffness may or may not be replaced by cramp at a later date. The attacks of cramp may occur several times every night, or as infrequently as an attack once a week. The commonest site of the cramps is in one of muscles or groups of muscles in the legs. The muscles of the hip, thighs and feet are also affected, but those of the arms and hands are rarely involved. These cramps are unlike tetany because they are asymmetrical in distribution, do not cause characteristic postures, and are not accompanied by accessory signs of irritability. There is a tendency for the cramp to recur in the same place. Each attack is acute and of short duration. The spasm in the muscles is brought on by the movement of the part after a period of rest. This is especially noticeable during the night, when, each time the patient moves in bed, the cramp comes on and the pain is so severe that it wakes her up. This complaint is therefore a source of restless nights, and even of insomnia, because the patient is afraid of not lying still. In the day-time the cramp comes on during walking and causes the patient to fall.

PROCEDURE.

Three types of treatment were carried out and a fourth group of patients were left without any treatment in order to provide controls. In all 198 cases were investigated. At first the sodium chloride and the calcium lactate were given to alternate patients. The difference between the results from these 2 treatments was such that it was then decided to use 2 sets of controls alternately with the sodium chloride, and there were 105 controls. Of these controls, 48 were given calcium lactate, 25 had saccharine tablets and 32 were left untreated.

The patients were seen and examined in the antenatal clinic. Treatment was begun the first time the patient came complaining of cramp. Treatment ceased either when the cramp was cured, or in the uncured cases, when labour began. The patients were followed up at each subsequent antenatal visit, and were finally interviewed in the maternity wards after delivery.

The treatments were as follows:
(1) Sodium chloride by mouth.
(2) Calcium lactate by mouth.
(3) Saccharine tablets by mouth.

MATERIALS.

Calcium lactate. This was used in the form of tablets containing gr. 5 of calcium lactate. Two tablets were taken by mouth with water 3 times a day.

Sodium chloride. At first, sodium chloride was used in powder form; gr. 60 was prescribed by mouth, with water twice a day after meals. The taste was objectionable. An attempt was made to disguise this with various flavourings, without success. Therefore, when 53 patients had

been treated with the sodium chloride as powder, a change was made to sodium chloride in tablet form. Forty patients were given these tablets. Each tablet contained 15 gr. of sodium chloride. One tablet was taken by mouth with water 3 times a day after meals.

Saccharine tablets. One tablet was taken by mouth 3 times a day after meals with water.

RESULTS.

The results are shown in Tables I and II.

Duration of treatment. In the cases where the cramps ceased before the end of pregnancy, the mean duration of treatment with both calcium lactate and saccharine tablets, was 3 weeks. The mean duration of treatment with sodium chloride was 1.5 weeks. In the cases that were cured the cramps ceased after 1 week's treatment in the following percentage of cases:

(1) With sodium chloride in 83 per cent.
(2) With calcium lactate in 43 per cent.
(3) With saccharine tablets in 40 per cent.

TABLE I.

Treatment	Calcium lactate	Controls Saccharine tablets	Untreated cases	Total cases	Sodium chloride Powder	Pills	Total
Number of cases ...	48	25	32	105	53	40	93
Cured	23	11	15	49	48	34	82
Improved	25	2	16	51	4	6	10
Unchanged	2	12	1	5	1	0	1
Recurrences	6	0	0	6	8	4	12

TABLE II.

Treatment	Calcium lactate	Controls Saccharine tablets	Untreated cases	Total cases	Sodium chloride Powder	Pills	Total
Toxaemias	10	7	5	22	7	2	9
Stillbirths	2	0	0	2	3	0	3
Premature infants	2	0	2	4	4	2	6
Primiparae	27	13	14	54	26	17	43
Multiparae	21	12	18	51	27	23	50
Previous toxaemias	0	1	1	2	2	0	2
Number of cases ...	48	25	32	105	53	40	93

Rate of cure. The cramps ceased before the end of pregnancy in 44 per cent of the patients who were given saccharine tablets, in 47 per cent of the patients who had had no treatment, and in 48 per cent of the patients who were given calcium lactate. The cramps ceased before the end of pregnancy in 88 per cent of the patients who were given sodium chloride; in 95 per cent of those who were given it as a powder, and in 85 per cent of those who were given it as pills.

In all but a very few cases, the cramps ceased when the infant was born.

Recurrences of the cramp. There were no recurrences among the cases who had not been given any treatment, nor in the cases who had been given saccharine tablets. There were 6 recurrences among the cases treated with calcium lactate, and 12 among the cases treated with sodium chloride. All but 2 of these 18 recurrences took place during hot weather. Of these 2, one occurred after a severe bout of diarrhoea

and vomiting, and the other occurred in winter in an otherwise healthy patient. Both of them had been treated with sodium chloride.

The subsequent course of the pregnancies. Harding and Van Wyck (1926) say that if salt is freely given in the diet of a normal pregnant woman its effects are neglible; if, however, there is a tendency to toxaemia the condition is intensified. Four of the multiparae in this investigation had had toxaemia in 1 previous pregnancy. In none of them did the toxaemia recur in the present pregnancy, even though 2 of them were given sodium chloride.

The percentage-incidence of the toxaemias was less among the patients who were given sodium chloride than among the patients who were given calcium lactate, saccharine tablets or no treatment at all. The percentage of premature births and stillbirths was about the same among the patients treated with sodium chloride as in the 3 control groups. The percentage of failures to establish lactation was the same in all 4 groups.

CONCLUSION.

(1) Treatment of the cramps of pregnancy with calcium lactate gives no better results than treatment with saccharine tablets.

(2) In 47 per cent of the untreated cases the cramps ceased before the end of pregnancy.

(3) There were 18 relapses in the whole 198 cases. The relapses in all but 2 cases, occurred in hot weather.

(4) Treatment with sodium chloride cures the cramps of pregnancy in a large percentage of cases. It has no ill effects on either the mother or the infant. It does not increase the incidence of the toxaemias of pregnancy. In 83 per cent of the cases cured the duration of the treatment was less than 7 days.

(5) The fact that an increased salt-intake cures the cramps of pregnancy may mean that these cramps are due to a deficiency in the adrenal gland (Richter, 1936); or may mean that an increase in salt-intake is necessary in pregnancy for the greater activity of the ovary (Thorn and Harrop, 1937).

(6) The cramps of pregnancy are apparently similar to the heat cramps in industry.

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Some Aspects of Foetal Pathology
(With Special Reference to the Role of Amniotic Bands)

BY

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"THERE is an impression very generally entertained in society, and especially among those whose experience or whose studies have made them but little conversant with the knowledge of disease, that

> . . . the thousand natural shocks
> That flesh is heir to . . .

is an inheritance on which we do not enter until we have breathed the breath of this world's life; and considering the peculiar circumstances of the child before birth, one would at first be inclined to conclude that although of course exposed to the risk of injury from accidents or disease occurring to the mother, it would not be liable to many or serious lesions of its own; yet observations and experience have fully and sadly revealed to us a very different state of facts, and force upon us the melancholy truth, that the seeds of life are often sown adultered with those of infirmity and decay; that disease may mutilate and death destroy long before our entrance into life: for, as far as past investigation has enabled us to reach, we have reason to believe that the unborn child is not only liable to certain affections peculiar to itself, but that it is also subject to almost all which affect the adult: and under this peculiar disadvantage, that, while for it there are indeed the *mille mortis viae*, there are not, unhappily, as yet added the *mille salutis.*"

Montgomery (1863) wrote the above sentence. The profundity of the truth therein expressed is even more evident to-day.

Review of Literature.

Chaussier (1812) had been the first to draw attention to amniotic bands. He is quoted by Simonart (1845) and Montgomery (1863). The latter states:

> " Chaussier, like most of his predecessors, attributes the accident of gangrene as the cause which would most obviously account for its production, though it does not appear from his account that there were present any of the pathological evidences of that condition; and, in the case first related, the child was born alive, and it is expressly mentioned that neither the stump of the limb nor the part amputated showed any symptom of disorganisation or disease, not being even discoloured."

Watkinson (1825) gives the first account in this country of a case of intrauterine amputation, but he does not record the presence or absence of bands. The left leg had been completely amputated a little above the ankle. The foot was found in the vagina in a state of good preservation (" nearly healed ") after the premature birth of the child at seven months.

Montgomery ascribes the cause of amniotic bands to inflammatory changes. Quoting Dr. Simpson of Edinburgh (1836), Montgomery (1863) says:

> ". . . he also assents to, and indeed strongly confirms my view, both as to the agent which produced the change and its consisting of organised lymph, such as is usually elaborated under the influence of inflammatory action, from which it is well known that several varieties of foetal deformities arise, and it is a matter of every-day observation, how completely lymph so effused will

be converted into distinct firm threads, uniting opposite serous surfaces, especially those which move freely on each other as the pleurae and the peritoneal coverings of the abdominal viscera."

Indeed, Simpson (1856) had gone further and had published an essay to show that:

" There takes place on the stumps of the limbs that have seemingly undergone an early spontaneous amputation *in utero*, a rudimentary reproduction of the amputated parts, in consequence of which, on the end of many such stumps, there is observable a projecting mass or nodule, varying in size from a small cutaneous ridge to the bulk of a walnut, and having protruding from its surface, one, two, or more still smaller fleshy divisions or projections, which are provided at their extreme points with nails; which fact he justly regards as highly interesting from being, as he believes it to be, an effort or tendency in the human subject towards the reproduction of a lost extremity, which we so frequently see accomplished, and with a great degree of perfection in several of the lower classes of animals, and especially in the Crustacea."

Chiari (1911) called the amniotic bands " Simonart's bands ", and he points out, " Braun (1854) had expressed the view for the first time that Simonart's bands were in reality abnormally disposed portions of the amnion itself." Chiari states:

" Microscopically, these bands consist of a wavy mass of amniotic connective tissue, exhibiting very few nuclei and no blood vessels; they are covered by amniotic epithelium which shades into the foetal epidermis."

No review of this subject would be complete without quotations from the observations of Ballantyne (1902):

" As a matter of fact, it cannot be said that any satisfactory explanation of the production of the so-called spontaneous amputations has yet been advanced. I believe that they are produced or initiated before the truly foetal period of antenatal life, and they are connected with maldevelopment of the amnion; further, I am hopeful that when

new light is thrown upon the exact mode or origin of the amnion in the human subject, the whole question of the teratogenic effects of anomalies in its development will receive illumination. Till that times comes we must be content to speak somewhat vaguely of amniotic action, adhesions, bands, and the like. At the same time, congenital amputations must, I think, be regarded as teratological rather than traumatic in their origin, as belonging to the pathology of the embryo rather than to that of the foetus."

At a later date, Ballantyne (1904) states:

" It is reasonable to expect that amniotic pressure without actual adhesions may in some instances be effective in teratogenesis. It is also quite conceivable that an adhesion may exist at an early period of development, and, having accomplished its pathological purpose, may then be absorbed or lost to view in the morbid process it has set up . . . The number of cases in which deformities of the extremities of almost all kinds have been ascribed to the action of the amnion is very large; but the instances in which bands or filaments or adhesions have been actually recognized are comparatively few."

Ballantyne, himself, had not met with an example of the variety of amniotic band " in which the adhesion is between some part of the foetus and the umbilical cord, or rather the covering of the cord."

The present day explanation of intrauterine amputation and annular constriction is that of Streeter (1930). He writes as follows:

" It may be stated that no evidence has been found that intrauterine amputation is due to amniotic bands or adhesions or other mechanical constriction. Amniotic bands do exist and are sometimes associated with malformations, but where this occurs the two participate in the same disturbance and the latter are not mechanically produced by the former. Structures that have frequently been mistaken for amniotic bands apparently fall into two categories: (*a*) macerated sheets of epidermis; (*b*) strands of hyalinized fibrous

tissue which are the residue of the localized areas of defective tissue and which are a part of our story . . . The writer finds that the preceding negative statement regarding the cause of intra-uterine amputation can be framed more easily and more definitely than an affirmative one stating just why and how it occurs."

Streeter goes on to postulate

" a normal disparity in the quality and vitality of the different tissues of the body and that this disparity is inherent in the germ-plasm and hereditarily transmitted . . . By the time of birth the adjustment has for the most part been made and one finds traces of the damage in the form of depressions, grooves, or healed stumps, occasion-ally with slender residual strands of defective hyalinized material still adherent to the affected regions. It is these that have been mistaken for amniotic bands.

Stander (1945) supports Streeter's ideas. DeLee (1938) does not commit himself, beyond the statement that "the amnion offers promise of great results from scientific investigation." Munro Kerr (1937) is equally terse.

This subject has an interest for ortho-paedic surgeons, and Bunnell (1944) writes :

" It is an old belief that some deformities are caused in utero. It was supposed that insufficient amniotic fluid resulted in compression, bending the extremities clubbed, and that constricting bands of amnion, adhesion or umbilical cord strangled limbs, resulting in the circular furrows found, and even in amputations. Bagg and others have shown definitely the fallacy of these theories. . . . Annular grooves and congenital amputations are not from intrauterine bands, but are merely ring-shaped defects."

I have consulted the work of Bagg (1924) and his observations were made after X-ray irradiation of animals in utero. He there-fore produced experimental lesions in normal tissues, a state of affairs not com-parable, or, at any rate, not directly applicable, to the present study.

Denis Browne (1936), in a discussion on "Congenital Deformities of Mechanical Origin", illustrates many cases of abnormal attitude of the foetus in utero, but he accepts the views of Streeter with regard to ring constrictions of the extremi-ties. He illustrates also " the foot of a new-born baby showing marks suggesting pressure sores."

Mall (1917), on the other hand, studied localized anomalies in human embryos and infants at birth, and states :

" It is perfectly clear that monsters are not due to germinal and hereditary causes, but are pro-duced from normal embryos by influences which are to be sought in their environment. . . . In any similar numbers of abortions localized anomalies should be noted twelve times as fre-quently as monsters at term."

Attention should be drawn to two inter-esting pre-war German papers, one by Gruber (1939) which has a most compre-hensive bibliography, and another by Cohrs (1939). The latter stresses that the large variety of amniotic abnormalities as met with in man is quite unknown in domestic mammals and birds.

Very recent animal experiments by Warkany (1944) have proved that maternal dietary deficiencies can induce congenital malformations in the offspring, e.g., cleft palate, syndactylism of the fingers and toes, as well as other skeletal changes.

This review must mention the work of Gregg (1941), of New South Wales, who discovered the relationship between mater-nal rubella in pregnancy and certain congenital malformations, such as cataract, in the infant born subsequently. His original observations have been extensively corroborated and amplified by Swan, Tostevin and Black (1946).

Finally, Wiener (1946) has indicated the possibility of at least one variety of spina bifida being produced by Rh sensitization.
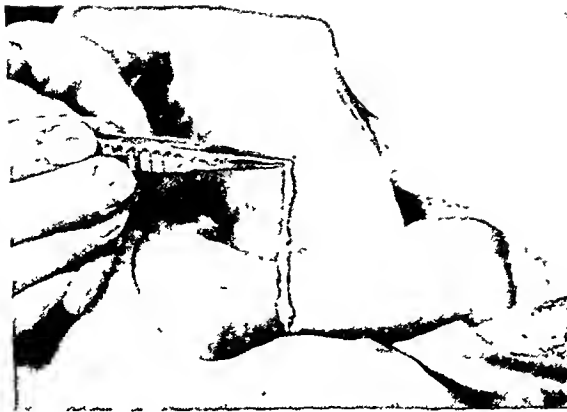
FIG. 1.

One end of amniotic band round annular constriction of leg as found at vulva.

(Case 1)

FIG. 2.

The raw annular constriction. (Case 1)

G.L.

Fig. 3.

Foetal aspect of placenta, showing cyst of
umbilical cord with other end of amniotic
band. (Case 1)

Fig. 4.

The healed annular constriction. Bilateral
varus deformity. (Case 1)

G.L.

| A | B |

Fig 5.

(A and B) Absence of digits
B " Rudimentary reproduction of amputated parts " (Case 2)
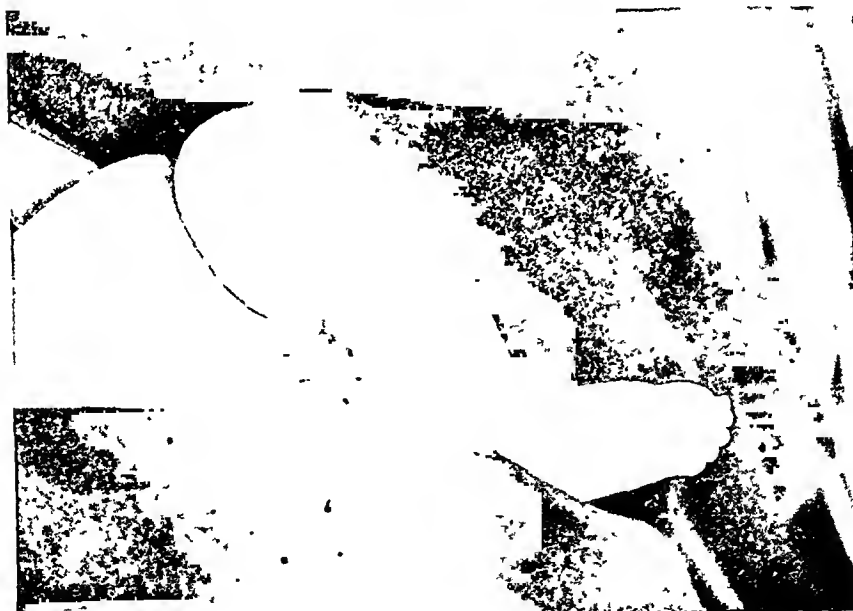
FIG. 6.
Annular constriction above knee. (Case 2)

FIG. 7.

Raw area on medial aspect of each ankle. (Case 3)
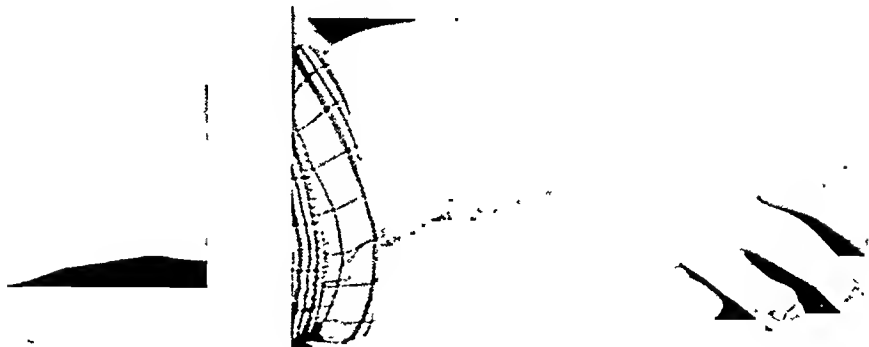
A   B

FIG. 8.

A. Left hand with no thumb.
B. Right hand with no thumb, abnormal nail beds, and absence
of forearm bone (either radius or ulna—X-ray not conclusive)
with flail elbow (Case 4).

G.L.

PERSONAL OBSERVATIONS.

CASE 1. Mrs. M. P., aged 24, o-para, was admitted as an emergency on November 10th, 1946, because she had a "show" of blood following attempts at version by her doctor. She was then 37 weeks pregnant.

On examination, urine and blood pressure were normal. The woman looked well. She had no oedema. The baby was small and presented by the breech. There was a normal amount of liquor amnii. The foetal heart was strong and regular. Painful uterine contractions were occurring. No attempt at version was made until the patient was anaesthetised when it was considered version would be easy. But it proved otherwise. The head could be guided easily round to the iliac fossa, but the breech, which was above the brim, would not move in any direction. Indeed, the head escaped from the hand at this point and resorted to the fundus of the uterus. A second attempt was made but this time, as soon as the head was guided round to the iliac fossa, the membranes ruptured and the presentation remained a breech. The foetal heart was satisfactory.

Three hours later I was "scrubbed-up" waiting to aid delivery, if required, when I noticed what I thought was a ligature (similar to white-string cord-ligature) hanging from the ankle of one of the presenting limbs. Closer inspection revealed this ligature (Fig. 1) around an annular constriction (Fig. 2) of the baby's leg. This band was easily detached. The constriction of the leg had a raw, granulating surface. Delivery of a living male child, weighing 4 pounds 9 ounces, was completed spontaneously by the mother. The placenta was examined carefully and showed an umbilical cord cyst, and a piece of amniotic band similar to that round the ankle (Fig. 3). In my opinion this band, when intact, caused the immobility of the breech above the brim during attempts at version.

The constriction healed in a few days (Fig. 4). Plaster fixation treatment was instituted for the bilateral varus deformity (Fig. 4). The child also had a naevus on the back. There was no X-ray evidence of spina bifida.

When seen 6 months later the child was well, and its feet were in good position. (It was then still having plaster treatment). The constriction was causing no disability. The baby seemed normal mentally.

The mother stated that she had no illness during the first three months of pregnancy, but that she had infective jaundice just prior to and during the conception date. She had contracted the jaundice from her brother who was ill with it on his arrival home from Salonika a short time before.

The mother's blood was Group A, Rh negative, and the baby's, Group AB, Rh negative. Coombs' test was negative.

CASE 2. A primigravida, aged 43, was admitted to hospital on September 11th, 1946, with a history of "heavy show." She was 38 weeks pregnant. She was not losing on admission. Blood pressure was 120/75, and the urine was clear. The head was above the brim in a right occipito-lateral position and the foetal heart was satisfactory. A few small fibroids could be palpated on the uterine wall near the fundus. The condition of the woman was excellent. She had no pain. Her blood group was A, Rh negative. No Rh antibodies had been detected on examination of the blood at the antenatal clinic on August 23rd.

X-ray pelvimetry the next day confirmed what had been found clinically, namely, contraction of the outlet. On September 14th a special type of X-ray was taken, from which the following report was made:

"*Abdomen*: High head. Foetus displaced forwards. There is possibly a posterior placenta, but in which case it is probably only of the marginal variety. No foetal abnormalities seen."

On September 19th the patient had another "show" of blood, and lower segment Caesarean section was performed. A male child, weighing 6 pounds 6 ounces, was delivered alive with grossly deformed hands (Fig. 5, A and B), an annular constriction above the right knee (Fig. 6) and bilateral varus deformity of both feet.

The placenta proved to be most interesting. It was large and situated on the posterior wall of the uterus. The lower part was definitely praevia, thus accounting for the "warning" haemorrhages. When removal of the placenta was attempted after the routine intrauterine injection of ergometrine (0.5 mg.), the upper portion was seen to be separated by retro-placental clot, but the lower half was truly placenta accreta. No plane of cleavage could be found. In view of the gross deformities of the

child, and despite the Rhesus factor, it was decided to try to conserve the uterus, and the accreta portion of the placenta was removed piecemeal with great difficulty. Blood transfusion was started. The uterus was packed with gauze, using DeLee's shuttle. At the end of the operation, the vagina also was packed. Penicillin and sulpha-drug therapy was instituted immediately. In 9 hours the vaginal pack was removed, and the uterine pack in 18 hours. There was no further haemorrhage and the patient's convalescence thereafter was smooth and without any notifiable pyrexia.

No amniotic bands were seen in this case. There was a normal amount of liquor amnii.

The patient has been seen 8 months later and her periods are painless, normal in amount, and regular. She has no complaints referable to her pelvic organs. She recalls that she was in bed for 5 days when just over 2 months pregnant with what her doctor called "food-poisoning", diarrhoea and vomiting.

The baby has completed plaster treatment for varus deformity. The result is good. Its blood is Group O, Rh positive. It appears normal mentally.

Case 3. Mrs. M., aged 20, o-para, had a normal spontaneous delivery at term in 1943. The baby was born with the lesions seen in Fig. 7, described as "injury on medial aspect of both ankles extending into deep tissues."

The pregnancy had been normal apart from slight rise in blood pressure and swelling of the ankles in the last 2 weeks. Both the mother's Wassermann reaction and the child's were negative. The Rh factor was not determined. The placenta was healthy and complete, as were the membranes. There had been no oligohydramnios.

For one week the lesions were treated with a bland ointment without improvement, then, after an initial débridement, the sites were enclosed in sterile Bunyan envelopes and irrigated with 2 per cent solution of sodium hypochlorite. In one week the left ankle had completely healed and granulation and epithelialization was well established on the right side. At this point the mother removed the child from hospital against medical advice.

Case 4. Mrs. M., aged 34, had had one miscarriage at 2 months. On February, 21st 1944, labour was induced at 39 weeks for pre-eclamptic toxaemia. At birth, the child had the deformities seen in Fig. 8, A and B. (Photograph taken when child was 3 years old).

Mrs. M. can recall no illness during the first 3 months of that pregnancy. There is no evidence that there was hydramnios or oligohydramnios. The child at 3 years of age is a healthy boy of normal intellect, who is overcoming the limitations of his deformity in the most amazing manner.

The mother's blood group is A, Rh positive, and that of the child, O, Rh positive.

A second child was born in February, 1946, and it is normal in every way.

DISCUSSION.

It would be advisable to restate briefly the theories already reviewed as to the causation of amniotic bands, intrauterine amputations, and congenital abnormalities.

1. Gangrene of part (Chaussier).

2. Inflammatory (Montgomery, Simpson).

3. Abnormal disposition of portions of amnion (Braun, Chiari).

4. Maldevelopment of amnion ± pressure. ("Teratological rather than traumatic." "Embryo rather than foetus." [Ballantyne].)

5. A normal disparity in quality and vitality of different tissues, inherent in the germ-plasm and hereditarily transmitted (Streeter).

6. Merely ring-shaped defects (Bagg, Bunnell).

7. Environmental influences (Mall).

8. Dietetic (experimental) (Warkany).

9. Rubella (Gregg).

10. Incompatible Rh Groupings (Wiener).

One feels that Chaussier and his successors failed to distinguish between cause and effect. One argument against an inflammatory cause is that microscopic section of the band in Case 1 showed no inflammatory reaction, and was in accord

TABLE I.

	Parity	Deformity	Mother's blood	Baby's blood
1.	o	Syndactilism Bilateral varus (Case No. 2).	Group A Rh negative.	Group O Rh positive.
2.	One normal since.	Syndactilism Absence of one bone in forearm (Case No. 4).	Group A Rh positive.	Group O Rh positive.
3.	o	Amiotic band Bilateral varus (Case No. 1).	Group A Rh negative.	Group AB Rh negative (Coombs test negative).
4.	8	Recurrent mental deficiency.	Group O Rh negative.	——
5.	o	Meningocoele Spina Bifida.	Group A Rh negative.	Group O Rh negative (Coombs test negative).
6.	o	Cystic kidney disease and other abnormalities.	Group A Rh negative.	Group A Rh positive (Coombs test negative).
7.	o	Anencephaly.	Group A Rh negative.	——
8.	Four normal previously.	Hydrocephalus.	Group A Rh positive.	——
9.	Two normal previously.	Anencephaly.	Group A Rh positive.	——
10	o	Anencephaly.	Group O Rh negative.	——

It has been shown experimentally that diet-deficiency will also cause foetal abnormalities.

On the clinical side, this subject is important in that antenatal supervision will have to begin earlier if the mysteries of foetal pathology are to be probed more fully. Further, the question of therapeutic abortion for possible foetal abnormality is raised by the known effects of rubella. Measures will be necessary to protect women against infection in early pregnancy. There is an immense field for exploration in the products of conception expelled at abortion.

Truly, "the first furrows are being ploughed in the wastes of foetal pathology" (Johnstone, 1947).

SUMMARY.

1. The literature of congenital malformations is reviewed, with special reference to the significance of amniotic bands.

2. Four cases are described, illustrating congenital abnormalities in living children. The presence of an amniotic band causing limb deformity has often been assumed but seldom seen: such a band is now recorded and illustrated.

3. In 8 of 10 cases of foetal abnormality the maternal blood was Group A. The Rh factor in the mother was negative in 7 of the 10 cases.

4. The classification of foetal pathology is discussed.

5. The clinical implications of the growing knowledge of foetal pathology are indicated.

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Inevitable, Incomplete and Septic Abortion

BY

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I AM writing this article to express my approval of the treatment of cases of incomplete abortion recently advocated by Corston and Stallworthy (1947); to support their dicta by an account of my own experience; and to make some criticisms. The treatment advocated is far from new. It has been the recognized method at the Rotunda Hospital to my personal knowledge for the past 50 years and it is the treatment described in every book written by a Master or Assistant of the Rotunda during this century.

During my 7 years of Mastership (1919–1926), 1,347 cases of abortion and early miscarriage were treated in the patients' homes; 502 cases were admitted and treated in the maternity wards; and during 5 years (figures for 2 are not available), 103 cases were treated in the gynaecological wards. These figures include only cases that ended with evacuation of the uterus and termination of the pregnancy, and all primarily applied or were admitted to the Hospital because of the active condition of some type of abortion. The cases treated in the maternity wards include a small number of miscarriages, chiefly early, that is, pregnancies with a history of 12 to 20 weeks' duration, in which the foetus had died but attained a size to be born first and followed by a placental third stage.

In the teaching of the Rotunda emphasis has always been laid on the importance of distinguishing between the abortion which comes away in a mass or in fragments and the miscarriage which has the definite 3 stages of labour and in which the third stage calls for management much as it does in labour at term. Cases with a development of pregnancy of from 18 to 24 weeks with the foetus born, the placenta retained, the patient bleeding, probably present as difficult a problem and as alarming an appearance when first seen as can be expected, and they offer little excuse for procrastination and postponement of active intervention, but such cases in the Rotunda district after they have been dealt with by hopeful but futile conservatism fall to the lot of the junior member of the staff " the Extern Assistant."

The relative number of the various types of case included in the above figures may be best estimated from the following statements in 2 early clinical reports. The nature of the cases applying to the Rotunda have not altered in any way since. " There were 64 cases of abortion treated in the hospital during the year and in no case was there any serious rise of temperature or other complication. In 9 cases the abortion was complete and needed no treatment. Severe haemorrhage occurred in only 5 cases. In the management of those cases which required treatment the flushing curette was generally used." " The cases of abortion and miscarriage were 64 in number, in 2 instances there was an insignificant rise of temperature, in 18 no treatment was needed, in 8 the bleeding

was severe." These figures suggest a very similar type of case to that dealt with by Stallworthy, who, of 600 cases, states "42 were frankly septic," whereas in the reports quoted above what is referred to as a serious rise of temperature is illustrated by the following: "One of these had a temperature rising on the fifth evening to 104.8°F." "One was admitted with a temperature of 101°F." "One had a roll of bandage in the vagina with a quantity of blood clot and a temperature of 102°F." "These 3 were the only cases of high temperature occurring." Again the conditions with regard to haemorrhage were probably also very similar. One of the above cases had been bleeding for 3 weeks, another had repeated haemorrhages for some weeks.

The line of treatment adopted in the Rotunda Hospital is well exemplified by the following quotations: "Some did not require any special treatment, only those in which the haemorrhage was severe, or in which any part of the ovum was still retained were interfered with. In all these cases the treatment adopted was the emptying of the uterus; if possible by expression of the contents. This failing, and the os being sufficiently dilated, the ovum was removed by the finger, or if the latter condition was not fulfilled, by Rheinstadter's Curette. In 1 case the cervix was cicatricial, it was dilated with Hegar's dilators and a 4 months' foetus extracted by means of Schultze's spoon-forceps. The patient's temperature rose on the evening of the 6th day to 104.6°F. and after a uterine douche fell to normal and remained so." "Another patient was admitted in the 4th month of pregnancy with a foetid discharge. The foetus could be felt in the dilated cervical canal. The external os was only the size of a threepenny-piece, it was divided bilaterally and the foetus extracted by Schultze's spoon-forceps. Free haemor-

rhage followed, the uterus was curetted and plugged with iodoform gauze. Convalescence normal."

In addition to the cases during my Mastership there were 777 cases treated in their homes, and 164 in the maternity wards during the 3 years that I was Assistant Master (1902–1905), making a total of 2,993; besides these there are the cases with which I have had to deal in private practice which have all been managed on the same lines as those in the Rotunda Hospital. All the cases referred to in the Rotunda were long before the advent of sulphonamides or blood transfusions, as were the great majority of my private cases. I have had no deaths in private practice and there were none in the early series (1902–1905) which were before even the adoption of intravenous saline, when reliance was placed on replacing fluid subcutaneously. There were 6 deaths; the following are the individual details.

CASE 1. Four months pregnant; bleeding for a week; refused to send to hospital. When first seen foetus born; patient bleeding severely. The placenta was retained but easily removed. The woman failed to respond to restoratives.

CASE 2. Three-and-a-half months pregnant; foetus born; placenta retained 3 days, easily removed. Temperature and pulse raised. Died on 26th day. Autopsy showed abscess of lung due to haemolytic streptococcal infection.

CASE 3. Admitted as incomplete septic abortion, uterus emptied with finger, uterine douche given. Signs of peritonitis developed. Vaginal hysterectomy done on 2nd day. Died on 3rd day.

CASE 4. Admitted as incomplete abortion, bleeding for a week; temperature raised. Uterus emptied with finger and douche given. Low morbidity, marked debility and anaemia. Went home against

advice 12th day, temperature 100°F. Died suddenly 2 days later.

CASES 5 and 6. Both miscarriages at 24th week; admitted with retained placentae. One died while being anaesthetized prior to manual removal. The other had rigors and temperature 103°-105°F. from first day and died on 11th day.

In my *Practical Midwifery* (1923) I say under "Threatened Abortion": "If any cause for the condition can be found it must be corrected at once if possible. Thus a retroverted uterus is replaced and supported by a pessary. It may not prevent the abortion. When the bleeding persists all discharge should be inspected for fragments of the ovum which would indicate the change to incomplete abortion. When the bleeding is moderately severe and persistent it may be an indication for emptying of the uterus and will nearly always be associated with a dead ovum. The bleeding is very seldom of sufficient severity to call for interference in the presence of a living ovum unless there is active uterine action which will undoubtedly terminate the pregnancy." Under "Incomplete Abortion" I say, "when a case is diagnosed as an Incomplete Abortion, either when first seen or after treatment as a threatened abortion, it is better to complete the emptying of the uterus at once." Under "Septic Abortion" I say, "there is only one rational treatment, and that is to clear out the cavity." I repeat these remarks in my *Obstetrics* (1937) but modify the first and say "the bleeding is never so severe as to require emptying of the uterus if the ovum is alive." This line of conduct implies the necessity of making a vaginal examination in the first instance: First, to establish the fact of pregnancy and to estimate its duration, which may not correspond to the history. Second, to define the condition and position of the uterus. Third, to ascertain the degree of dilatation of the cervix and

the extent to which the uterus has evacuated its contents. Then if the condition is considered inevitable or incomplete, whether it is suspected of being septic or not, the uterus is evacuated in the patient's own home without delay or she is moved into hospital for evacuation. Stallworthy says "failure to make this preliminary examination can result in the soft wall of a pregnant retroverted uterus being perforated." How anyone could contemplate passing any instrument without first defining the position of the uterus is difficult to conceive, while the omission of this examination prevents a differential diagnosis. Further, he says, in connexion with septic cases: "If haemorrhage was severe the patient was taken to the theatre without further delay: if it was not severe operation was postponed for 12 to 24 hours to obtain concentration of sulphonamides." Such a line of treatment is inconsistent with the theme of his paper, nor are there any definite signs indicated by which the fact of sepsis being present is established. It would not be reasonable to claim that all cases with fever are septic and recover only by virtue of the sulphonamides, nor could such be held in face of the cases I have cited. In private practice I have followed the same line of treatment; either evacuating the uterus in the patient's own home without delay if the condition found on examination indicated that such treatment could be effected easily, or I have moved the patient into a nursing home, usually in my own car, and evacuated the uterus without delay. If the patient has bled severely or was continuing to bleed severely I have not infrequently given an anaesthetic (chloroform) myself rather than delay when I have had difficulty in finding an anaesthetist.

I have never regretted immediate action as an alternative to permitting further loss of blood. In such a case the cervix will

usually admit the finger but if not is always easily dilated to 14 to 16 mm., which will admit a finger, while less will admit the only form of curette that should be used, a Rheinstadter's blunt flushing curette or spoon, carrying a free flow of fluid with a pressure not greater than that produced by a 12-inch head. A Rheinstadter's curette has no cutting properties, it scrapes the surface and hooks and flushes loose material out of a cavity. The majority of patients, when the uterus has been emptied and rubbed up bimanually, cease to bleed, just as after · manual removal of the placenta, and the uterus does not require to be plugged. In my books I say plugging should be removed within 6 hours and septic abortions should not be plugged. The patient is better for being allowed out of bed for all necessities afterwards, allowed to sit up next day and go home on the third or fourth day. Iron and ammonium citrate, gr. iii thrice daily, will restore the blood loss in the next few weeks as rapidly as can be and is the maximum dose of iron that can be absorbed; it is better continued for a couple of months and in such doses will not cause gastric disturbance.

Stallworthy refers to venous spasm as evidence of extreme blood-loss or shock. In my opinion such spasm is evidence of full compensation for the loss incurred and maintenance of same by vasoconstriction and therefore there is no anaemia of the brain centres. The essential in treatment is to stop further loss and if this is effected before the vasomotor centre suffers from anoxaemia balance will be fully maintained. On the other hand if delay allows anaemia of the centre to develop vasoconstriction will fail and the resulting fall in pressure, although it will probably stop the bleeding, leaves the patient in a pre-carious state from failure of the autonomic system. Blood transfusion may maintain a balance, it may also restart the bleeding and the blood be lost as rapidly as it is introduced; little is gained until the bleeding is stopped. In the same way oxytocic drugs produce a forced activity of the vasomotor centre but their local action is by contracting the bleeding site and this is ineffective if the site is not clean or the cavity is not empty; therefore when their action passes off the subsequent collapse is the greater. The one essential is to stop the bleeding before the vital centres are affected and then they will maintain full compensation. In the *British Medical Journal* (2.8.47), in the answer under the heading "Removal of Placenta", the advisability of giving ergometrine is queried and it is stated: "Usually it produces immediate separation of the placenta which can then be expressed. If, however, the placenta does not come away at once manual removal has to be carried out without delay." Obviously the reason for this is that the drug has promoted bleeding by separating the placenta, and delay risks the imprisonment of the placenta by hour-glass contraction, while the drug does not control the loss. The same applies to the action of this drug in the treatment of abortion, except that the forced uterine action may complete the emptying of the cavity and so the bleeding will cease. This paper is largely composed of quotations but I will close with one more from Purefoy's Clinical Report for the year 1902-1903. "It is not a little surprising how uncertain and timid most modern obstetric writers are in giving instructions as to the treatment of inevitable abortion and miscarriage. Masterly inactivity on the part of the physician cannot be too strongly condemned in these cases."

H

The Incubation Period of Ophthalmia Neonatorum

BY

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EVEN in the pioneer days of Neisser and Crede in the two penultimate decades of the last century, there was considerable doubt whether the gonococcus was the only causal agent of ophthalmia neonatorum. By the beginning of this century it was clearly recognized that ophthalmia neonatorum is caused by a variety of organisms, whilst the classical work of Halberstaedter and Prowazek in 1907, and of Stargardt in 1909, indicated the possibility of an ultra-microscopic virus as yet another causal agent. It would appear that the gonococcus was indeed the dominant causal organism towards the end of the last century and the beginning of this (Stephenson, 1907), but that the incidence of gonococcal ophthalmia neonatorum has declined considerably during the past 50 years or so. To-day the gonococcus is no longer the dominant causal agent; it accounted for no more than 180 of a consecutive series of 737 cases recorded elsewhere (Sorsby, 1945). *Staphylococcus aureus* would appear to be a more common exciting factor, and it is likely that, the virus of inclusion blennorrhoea is as common.

The change in the relative significance of the different causal agents of ophthalmia neonatorum raises the question whether the accepted teaching that ophthalmia neonatorum generally develops within the first 5 days after birth—a view elaborated when the gonococcus was the dominant causal agent—is still valid. To assess this validity, a consecutive series of 312 cases of ophthalmia neonatorum seen at the Ophthalmia Neonatorum Unit at White Oak Hospital during part of 1944, the whole of 1945 and 1946, and the early months of 1947, was studied. Information was sought as to the day of onset of the infection in the infants admitted, and this was correlated with the bacteriological and cytological examinations carried out. In 7 cases the records were incomplete in one or other respect, and there were 15 cases previously treated unsuccessfully elsewhere. These were eliminated from consideration so that the total was reduced to 290 cases. There were also excluded 5 cases occurring after 21 days (1 case each on the 22nd, 23rd, 26th, 35th, and 44th days).

FINDINGS.

Day of Onset in the series as a Whole.

Table I sets out the findings in these 290 cases. It will be seen that these cases fall into 4 distinct groups. In 179 cases organisms only were found; in 67 cases both inclusion bodies and organisms were found; in 15 cases neither organisms nor inclusion bodies were observed, and in 29 cases there were inclusion bodies only. In no cases was ophthalmia observed on the day of birth, whilst each of the days from the 1st to the 14th inclusive contributed a substantial quota with occasional cases occurring on the 16th, 18th and 21st day.

Fig. 1 shows the percentage-frequency on each day from the 1st to the 21st. Taking the series as a whole, it can be seen that 119 cases (41.03 per cent) occurred on the 1st to the 5th day, and 126 (43.45 per cent)

on the 6th to the 10th day; 35 cases (12.1 per cent) were observed on the 11th to the 15th day, and 10 (3.4 per cent) on the 16th day to the 21st. There is, therefore, concentrated in the first 10 days no less than 84.5 per cent of the total of cases, and there is little difference between the first 5 days of life and the subsequent 5 days. Assessed against individual days, the maximum incidence occurred on the 7th day (16.5 per cent) whilst the 3rd and 5th day contributed 11.0, 8.9, and 9.6 per cent of cases respectively. The 10th day still contributed 7.6 per cent of cases, with a rapid falling-off on the subsequent days.

Day of Onset in the 4 Main Groups.

As can be seen from Table II the day of onset in the group in which organisms only were observed differed from the series as a whole. In the 179 cases with organisms only 50.3 per cent occurred between the 1st to the 5th day, and 38.5 per cent from the 6th to the 10th day. In contrast, the corresponding percentages from the 67 cases showing both organisms and inclusion bodies were 31.3 and 50.7—a definite shift towards the 6th to 10 day. In the 29 cases with inclusion bodies only, this shift becomes still more marked, whilst substantially the same relationship is seen when the series of 29 cases is combined with a further group of 25 cases recorded previously. (Sorsby, Hoffa, and Young, 1944); only 16.7 per cent of cases occurred in the first 5 days of life and 55.5 per cent were concentrated in the 6th to the 10th day.

The group of 15 cases in which neither organisms nor inclusion bodies were found

FIG. I.

Frequency of onset on the different days after birth in the series as a whole.

Onset on	No. of cases.	Percentage of total.
1st day	12	4.14
2nd day	21	7.24
3rd day	32	11.03
4th day	26	8.97
5th day	28	9.65
6th day	19	6.55
7th day	48	16.55
8th day	23	7.93
9th day	14	4.83
10th day	22	7.59
11th day	10	3.45
12th day	10	3.45
13th day	6	2.07
14th day	9	3.10
15th day	-	-
16th day	2	0.69
17th day	-	-
18th day	2	0.69
19th day	-	-
20th day	-	-
21st day	6	2.07
	290	100.0
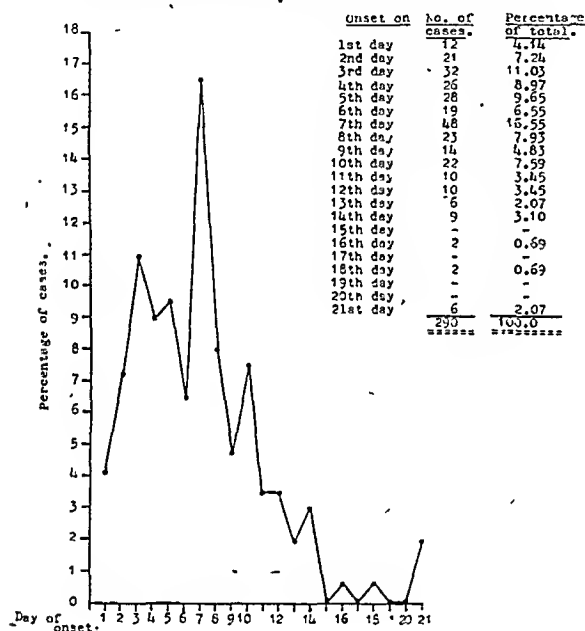
TABLE II.

Showing Days of Onset in the Series as a Whole and in the 4 Main Groups.

Onset on day of life	All cases		Organisms only		Organisms and inclusion bodies		Neither organisms nor inclusion bodies		Inclusion bodies only		Inclusion bodies only, incorporating 25 cases recorded previously	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	per cent
1st to 5th	119	41.03	90	50.28	21	31.34	4	26.67	4	13.79	9	16.67
6th to 10th	126	43.45	69	38.55	34	50.75	7	46.67	16	55.17	30	55.55
11th to 15th	35	12.07	16	8.94	9	13.43	3	20.00	7	24.14	12	22.22
16th to 21st	10	3.45	4	2.23	3	4.48	1	6.66	2	6.90	3	5.56
		100.0		100.0		100.0		100.0		100.0		100.0
	290	(100.0)	179	(61.73)	67	(23.10)	15	(5.17)	29	(10.00)	54	

is too small to lend itself to statistical assessment. If the day of onset is to be regarded as the last day of the incubation period, there is, therefore, a sharp difference in incubation period in the cases with organisms as contrasted to those in which inclusion bodies are present. The intermediate percentage obtained for the group with both organisms and inclusion bodies suggests that in most of these cases the organisms found are indeed the causal factors, although in a minority they are probably non-pathogenic so that the ophthalmia observed in these infants is in fact a virus blennorrhoea.

Day of Onset in Relation to the Commoner Causal Organisms.

Confining attention to the 179 cases in which organisms only were found, it will be seen that the pneumococcus, Koch-Weeks bacillus, Streptococcus viridans, Bacillus friedländer, haemolytic streptococcus, non-haemolytic streptococcus, and the Morax-Axenfeld bacillus are only occasional causal factors; together they account for only 22 cases. The remaining 157 cases include 51 of Staphylococcus aureus, 45 of diphtheroids, 36 gonococcus and 25 Staphylococcus albus. As can be seen from Table III and Fig. 2 the day of onset for these 4 organisms differs considerably. With the gonococcus 26 out of 36 cases (72.2 per cent) occurred within the 1st to 5th day and only 9 cases (25 per cent) during the period 6th to 10th day. In con-

trast there was an almost even distribution for each of these 2 periods in cases with S. aureus, 19 cases (37.2 per cent) and 20 cases (39.2 per cent) respectively. The distribution for diphtheroids was intermediate between that observed for the

FIG. 2.
Distribution as to day of onset in relation to the commoner causal organisms.
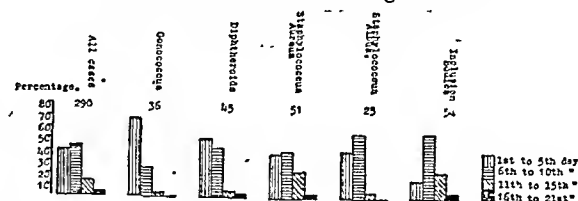
gonococcus and the S. aureus (48.9 per cent during the first 5 days and 42.2 per cent during the second 5 days of life). Cases with S. albus showed a rather greater incidence in the second 5 days than in the first (56 per cent and 40 per cent respectively).

Day of Onset in Relation to Severity of Affection.

It will be seen from Table IV and Fig. 3 that out of the total of 290 cases, 149 (51.4 per cent) were of moderate severity; there were rather more mild cases than severe ones, the respective percentages being 27.9 and 20.7. Contrasting the cases with onset from 1st to 5th day with those with the onset in the 6th to 10th day the distribution of mild, moderate and severe reactions is somewhat different; there are fewer severe cases in the second time-period, 21 out of

TABLE III.
Showing Days of Onset in Relation to Each of the Commoner causal Organisms.

Organism	Total	1 to 5 days		6 to 10 days		11 to 15 days		16 to 21 days	
		No.	per cent	No.	per cent	No.	per cent	No.	per cent
Gonococcus	36	26	72.22	9	25.00	1	2.78	—	—
Diphtheroids	45	22	48.89	19	42.22	3	6.67	1	2.22
Staphylococcus aureus	51	19	37.25	20	39.22	11	21.57	1	1.96
Staphylococcus albus	25	10	40.00	14	56.00	1	4.00	—	—

TABLE IV.

Showing Severity of Affection in Relation to day of Onset.

Onset on day of life	All cases		Mild		Moderate		Severe	
	No.	per cent	No.	per cent	No.	per cent	No.	per cent
1st to 5th	119	100.0	28	23.53	59	49.58	32	26.89
6th to 10th	126	100.0	35	27.78	70	55.55	21	16.67
11th to 15th	35	100.0	14	40.00	14	40.00	7	20.00
16th to 21st	10	100.0	4	40.00	6	60.00	—	—
Total	290	100.0	81	27.93	149	51.38	60	20.69

126 (16.7 per cent) against 32 out of 119 (26.9 per cent) in the 1st to 5th days. This difference is, however, not significant statistically, so that it may be assumed that there is nothing to suggest that ophthalmia

FIG. 3.

Severity of affection in relation to the commoner causal organisms.
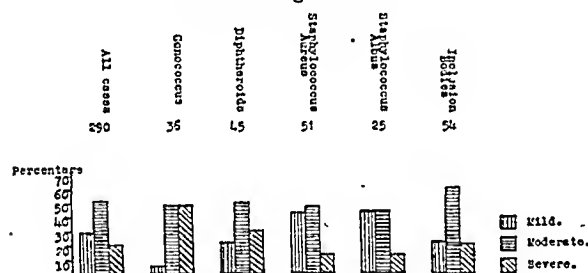
neonatorum developing from the 6th to the 10th day is likely to be less severe than instances of the affection developing earlier. Taking Table IV as a whole it would however, appear that there is a slight shift of the more severe cases towards the first 5 days of life.

Severity in Relation to Causal Organisms

Summary Table V and Fig. 3 show that the highest proportion of severe cases occurs when the infecting organism is the gonococcus: 17 in a series of 36 (47.2 per cent). A distinctly smaller proportion of severe cases is seen with the diphtheroids: 13 out of 45 (28.9 per cent). *S. aureus* gives a low incidence of severe cases, 6 out of 51 (11.8 per cent); and a similar low incidence is observed with *S. albus,* 3 out of 25 (12 per cent). Ophthalmia neonatorum with inclusion bodies appears to lie intermediate between the gonococcus and diphtheroids on the one hand and staphylococci on the other: there were 10 severe cases in a series of 54 (18.5 per cent). Mild cases appear to be exceptional with the gonococcus.

DISCUSSION.

Validity of the material.

The material recorded here may be taken as representative. Not all babies with ophthalmia neonatorum in London are

TABLE V.

Showing Severity of Affection in Relation to Each of the Common Causal Organisms.

Organism	Total	Mild		Moderate		Severe	
		No.	per cent	No.	per cent	No.	per cent
Gonococcus	36	2	5.56	17	47.22	17	47.22
Diphtheroids	45	10	22.22	22	48.89	13	28.89
Staphylococcus aureus	51	22	43.14	23	45.10	6	11.76
Staphylococcus albus	25	11	44.00	11	44.00	3	12.00
Virus, presumed from presence of inclusion bodies	54*	12	22.22	32	59.26	10	18.52

* Including 25 cases recorded previously.

admitted to White Oak Hospital; many receive treatment in obstetric units. There is, however, no special selection as regards admission. To eliminate the possibility of the series being loaded with resistant cases admitted for in-patient treatment, the 15 cases which were treated prior to admission to White Oak Hospital were excluded.

Validity of Bacteriological and Cytological Findings.

It is generally assumed that diphtheroids and S. albus are contaminants rather than exciting organisms. This is probably true of S. albus, particularly when the organism is coagulase-negative. As for diphtheroids, the fact that cases thus infected are somewhat resistant to penicillin therapy (Sorsby, 1947) strongly suggests that these organisms are of positive significance. Whilst the data on cases with S. albus have to be treated with some reserve, it may be taken that those for other organisms are valid.

Incubation Period in Ophthalmia Neonatorum at present.

The evidence submitted shows that the incubation period for ophthalmia neonatorum must be regarded as extending up to the 10th day. The cases seen after the 10th day—and these fall off rapidly—are probably examples of secondary infection. "Late" cases were well known and somewhat puzzling to the older observers (Stephenson, 1907) who were right in stressing the secondary character of some of these infections, but wrong in assuming that all cases after the 4th to 5th day were accidental infections. The occurrence of a considerable number of cases due to diphtheroids, S. aureus and the virus of inclusion blennorrhoea, with their large quota of infection setting in on the 6th to 10th day, as also the fact that some 20 to 25 per

cent of all cases of inclusion blennorrhoea occur on the 11th to 15th day shows that cases of ophthalmia neonatorum due to organisms other than the gonococcus tend to develop late. It is of interest to note that in the present series the gonococcal cases occurred predominantly in the first 5 days of life.

Degree of Severity in Ophthalmia neonatorum at Present.

Most cases seen are of moderate severity, but the highest proportion of severe cases occurs with the gonococcus. With this organism mild cases are unusual, and the incidence of severe cases equals that of moderate cases. With the other exciting organisms moderate cases predominate though diphtheroids and inclusion bodies give a substantial quota of severe cases. A severe case observed during the first 5 days of life has, therefore, a great probability of being due to gonococcus. Severe cases seen in the second 5 days of life are more likely to be due to diphtheroids or the virus of inclusion blennorrhoea.

Late Cases.

Of the 290 cases, 45 (15.5 per cent) occurred after the 10th day, mostly between the 11th and 15th day, 35 cases (12.1 per cent). It is likely that some of these cases are the result of extragenital infection, rather than cases of ophthalmia neonatorum in the strict sense. The marked fall in the number of cases with onset after the 10th day would suggest that the 10th day may be regarded as the upper limit of the incubation period, but the presence of inclusion bodies in no less than 21 out of the 45 cases with late onset, would seem to indicate that some of the late cases are indeed genital infections caused by the virus of inclusion blennorrhoea. On the other hand the occurrence of secondary

infection cannot be doubted. This was well shown in 2 cases in the present series. Two infants with unilateral infection due respectively to the gonococcus and diphtheroids responded satisfactorily to penicillin administered systemically. However, the second eye became involved on the 2nd and 3rd day after cessation of treatment, and the respective organisms were recovered from the eyes affected. Both these infants had been nursed by their mothers. Some of the " relapses " seen after treatment are probably also examples of a secondary, extragenital infection.

SUMMARY.

A consecutive series of 290 cases of ophthalmia neonatorum is recorded. Of this total 84.5 per cent occurred within the first 10 days of life; there were rather fewer in the first 5 days of life than in the second. The incubation period varied with the exciting organism. With the gonococcus some 70 per cent were observed in the first 5 days of life, with diphtheroids some 50 per cent and with S. aureus some 37 per cent, whilst with the virus of inclusion blennorrhoea there were only occasional cases in the first 5 days of life. As to severity, cases of moderate severity predominated in the series as a whole, but with gonococcal infections severe cases were as common; severe cases were infrequent with S. aureus. There was nothing to suggest that in an unselected series severe cases are substantially less frequent in the second 5 days of life than in the first.

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Further Observations on the Basal Temperature in Sterile Women

BY

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In the opinion of all investigators the two most important causes of female sterility are tubal occlusion and failure of ovulation in women who menstruate normally.

While the diagnosis of tubal occlusion is now easy, thanks to the Rubin test and to salpingography, the investigation of ovarian activity still offers many difficulties.

Among many methods used for this purpose, endometrial biopsy has been considered the most reliable.

During the last few years Rubenstein and Lindsley (1937), Zuck (1938), Barton (1940), Davis (1946), and others in the American literature, Tompkins (1945), Barton and Wiesner (1945a), and Halbrecht (1945), in the British, and Palmer (1943), in the French literature have reported observations of the cyclic temperature-curve in normally menstruating women—the phenomenon observed by Van de Velde more than 40 years ago—and they suggest the use of this to study the activity of the ovaries.

The results of their observations in thousands of cases have established the reliability of this method. Our own studies of 425 sterile women who measured their temperatures in 1,184 cycles, not only confirm those results, but have also enabled us to observe certain characteristics of these temperature-curves that had hitherto remained unnoticed.

These variations of the basal temperature-curves of sterile women seem to us to be not accidental but very significant.

Variations of the Bi-phasic Curves.

The length of the premenstrual phase (we purposely do not call it the "luteal phase", because we do not yet definitely know how the rise in temperature in this phase is influenced by the corpus luteum) in relation to the postmenstrual phase is more or less constant, although variations of 2 to 3 days are not rare in the same woman. Generally the premenstrual phase varies between 10 to 16 days. Short premenstrual phases of 6 to 9 days are generally rare. They recur frequently, however, in the same woman. Still less frequent are long phases of 16 to 18 days. A temperature that remains elevated for longer than 20 to 22 days definitely indicates pregnancy. In those rare cases in which bleeding occurs about 22 days after the beginning of the second phase we are probably dealing with an early abortion rather than with delayed menstruation (Fig. 1).

The differential diagnosis of delayed menstruation and early abortion is especially important when considering the proper therapy for infertility. In many cases the

FIG 1
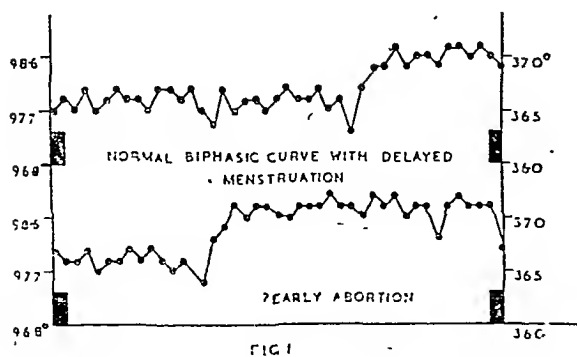
FIG 2

temperature remains at about the same level in both halves of the cycle. The halves are, however, separated by a drop in temperature lasting 1 to 3 days (Fig. 2).
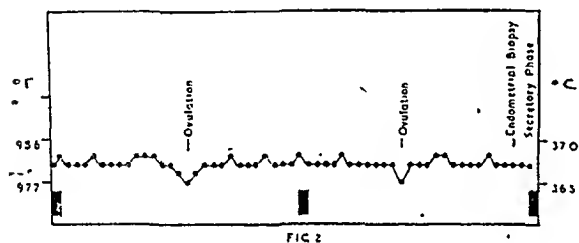
This drop in the temperature-curve seems to coincide with the time of ovulation but is not followed—as is normally the case—by an elevation of temperature. The assumption that this variation of the curve is to be considered as being bi-phasic and that it permits the diagnosis that ovulation has taken place was confirmed by endometrial biopsies at the end of many such cycles.

High and Low Basal Temperatures.

In 80 per cent of the women investigated, the oral basal temperatures varied between 36.4 and 36.8°C. in the postmenstrual phase and between 36.9 and 37.2°C. in the premenstrual phase of the cycle.

Fifteen per cent of the women had constantly a morning oral temperature below 36.4°C. in the postmenstrual phase, in many cases even below 36°C., and a corresponding elevation in the premenstrual phase. These low temperatures remained at the same level during the whole period they were measured and were not influenced by any hormonal or thyroid therapy (Fig. 3).

We could find no connexion between these low temperatures and the basal metabolic rates. On the contrary, we found the basal metabolic rate to be somewhat elevated, varying between plus 2 and plus 28, in 35 cases of low temperatures in which we measured the basal metabolic rate. It seems to be a matter of individual constitution rather than a symptom of hormonal dysfunction.

Rarer were the cases of patients with constantly elevated temperatures who measured above 37°C. in the postmenstrual phase and 37.3 to 37.5°C. in the premenstrual phase (Fig. 4).

FIG 4

FIG 3
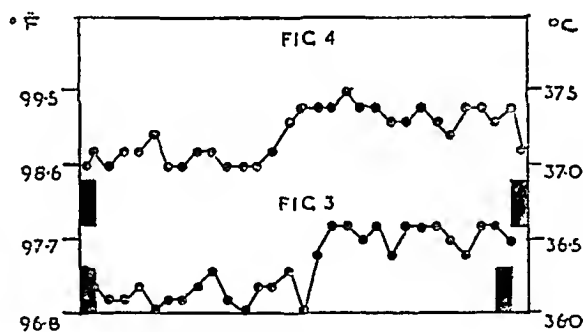
In all these cases which amounted to no more than 5 per cent of the total number investigated, we could find no organic reason for the elevated temperature.

This variation of temperature curve could not be influenced either by hormonal—estrogenic therapy. Their basal metabolic-rate was normal. This too seems to point to a constitutional factor.

The Influence of Hormone Therapy upon the Basal Temperature.

Most investigators ascribe the elevation of the temperature during the second half

of the cycle to the influence of the hormone produced by the corpus luteum. Barton and Weisner (1945b) seem to have succeeded in getting the same result artificially by injecting progestin.

Our own experiments lead us to results different from those of other investigators:

1. Daily injections of 10 mg. progestin did not produce any elevation of temperature in an apparently healthy male.

2. In 28 women who had normal biphasic temperature-curves, we obtained the following results after injecting 10 mg. of progestin every other day beginning with the 15th day of the cycle.

(a) In 11 women we succeeded in advancing the menses by 4 to 8 days; and the premenstrual phase, with the elevation of temperature, seemed to be shortened (Fig. 5).

FIG. 5
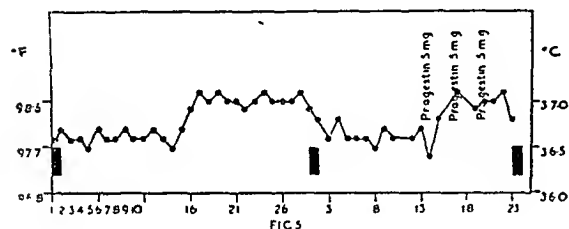
(b) In 4 other women who had biphasic temperature-curves before starting the injection of progestin, the curves changed to the monophasic type and the menses were advanced about 6 to 8 days (Fig. 6).

FIG. 6
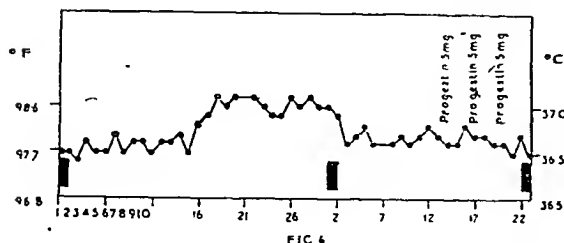
(c) In 6 women with monophasic cycles the temperature-curves remained uninfluenced in spite of large doses of progestin (Fig. 7).

FIG. 7
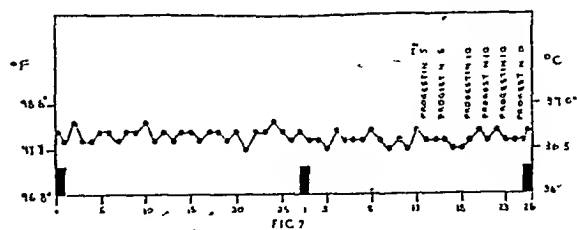
(d) Only in 1 case the temperature rose after progestin, causing an otherwise monophasic cycle to become biphasic (Fig. 8).

FIG. 8
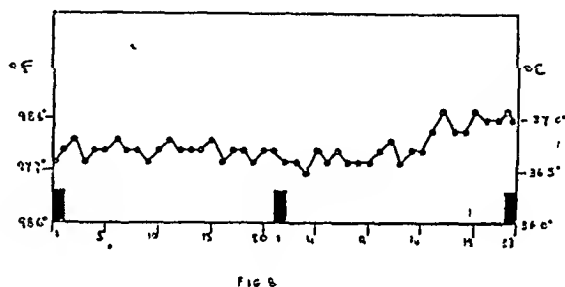
Thus we could not find a case in which progestin had a positive influence on the temperature-curves. The negative results we observed in 4 cases seem to have been caused by the early event of the menses before ovulation could take place. All this leads to the conclusion that the rise in temperature during the second half of the cycle, although hormonal in character, is not caused by a pyrogenic influence of the corpus luteum. The mechanism of the elevation of temperature in the premenstrual phase is probably more complex. We have not succeeded in lowering the temperature by using oestrogens, as some investigators report; nor did we succeed in influencing the basal temperature by the use of thyroid preparations.

The Monophasic Curves.

In 222 cycles investigated (19.5 per cent) the temperatures were monophasic. These cycles have to be considered as being anovulatory. The result of measuring

temperatures during a single cycle only is not sufficient to determine the ovarian functioning. Anovulatory cycles are not rare even in otherwise normal and fertile women. A questionnaire answered by 250 pregnant women showed that 52 of them had conceived only after 3 to 12 months of normal cohabitation, this permitting the assumption that at least some of them had anovulatory cycles.

The monophasic curve in a single cycle does not mean anything more than that the particular cycle is anovulatory. It is necessary to measure the basal temperature of at least 3 cycles in order to determine accurately the woman's true fertility. The longer a woman measures her temperatures the more accurate will be the determination of her chances of pregnancy (Fig. 9).
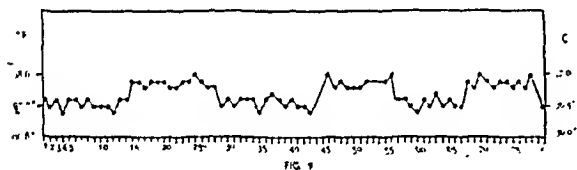
FIG. 9

Fig. 9 shows that among the 128 women who measured their temperatures during a single cycle only, 32, that is, about 27 per cent, had monophasic curves, whereas the percentage of completely anovulatory women tends to become smaller the longer the temperatures are measured; that is, about 18 per cent if they measured 2 cycles and only 3 per cent if measured during 4 cycles.

The number of normally menstruating women who do not, sooner or later, have a spontaneous ovulation is also very small. This explains the fact that many women become pregnant, without treatment, after being sterile for many years. As mentioned before, we used the basal temperatures as an indicator of the efficacy of our therapy. Only rarely did an ovulation follow hormonal therapy (pregnant mare's serum, etc.). More often was this the case after X-ray therapy to the ovaries and the hypophysis.

The Basal Temperature in Cases of Amenorrhoea.

In 13 cases of amenorrhoea the temperature was monophasic during 2 or 3 months. In 2 other cases where the measuring of temperatures was continued for 4 to 5 months until the menses appeared spontaneously, the temperature rose during the last 14 days, thus becoming biphasic. This phenomenon explains those cases of pregnancy that occur during a period of amenorrhoea.

In 1 case of primary amenorrhoea biopsy showed an atrophic endometrium and tuberculous endometritis. The temperature-curve of this woman nevertheless showed a cyclic biphasic rhythm (Fig. 9).

It is therefore possible that this patient ovulates every 4 weeks without participation of the endometrium in the process. On the other hand, it is possible that the biphasic rhythm of the temperature is influenced by other factors as well.

Basal Temperature and Endometrial Biopsy.

In 90 cases we were able to compare the basal temperatures with endometrial biopsies taken during the same cycle. In all but 3 cases the results were identical. In 1 of these 3 cases the temperature-curve was monophasic while the endometrium was, in part at least, in the secretory phase. In the other 2 cases the curve was biphasic while the endometrium was quiescent. One of these women became pregnant after a few months.

On consideration it seems that the basal temperature is more reliable than the endometrial biopsy, at least for the purpose of

determining the time of ovulation. Our reasons are as follow:

1. Biopsy allows investigation of only a small part of the endometrium and it is known that the endometrium does not react uniformly in all its parts to hormonal stimuli.

2. It is easy to continue measuring temperatures during a long period, whereas it is difficult, and not without danger to the patient, to repeat the endometrial biopsy frequently.

3. Only 46 out of 1,184 curves (less than 3 per cent) were unusable, whereas the number of biopsies that do not permit a definite interpretation is much larger.

The Technic of Measuring Basal Temperatures.

There is no practical différence in reliability between the oral, rectal or vaginal temperatures and most patients prefer the oral method. The axillary measurement, however, is quite unreliable.

The best time to measure the temperature is in the morning before rising. It is particularly important to insist upon its being done before the woman leaves the bed, a point which is frequently disregarded. A few minutes after leaving bed the temperature will show a drop of °F. (0.1 to 0.3°C.) and not until later, after physical activity, does it rise again.

SUMMARY.

1. The basal temperature-curves in 1,184 cycles of normally menstruating sterile women were definitely biphasic and in 23 cases, probably so. On the other hand, 222 cycles were monophasic and in 46 cases the curves had to be discarded.

2. Temperature-curves allow us not only to diagnose very early pregnancy, but also to differentiate between delayed menstruation and early abortion.

3. In many women, ovulation seems to effect no more than a drop of 0.1 to 0.3°C. during 1 to 3 days of the intermenstrual mid-cycle without any elevation of temperature in the premenstrual phase above the postmenstrual phase.

4. About 15 per cent of all women investigated, had temperatures below 36.4°C. in the postmenstrual phase and a correspondingly elevated temperature in the second half of the cycle. Five per cent of the patients invariably had temperatures above 37°C. These high and low temperatures seem to be constitutional and cannot be influenced by hormones.

5. Thyroid extract, progestin, and oestrogens do not change the temperature-level. The rise in temperature in the second half of the cycle is caused by a complex mechanism, lutein being probably only one of the many factors.

6. Amenorrheic women have monophasic curves. In many cases, however, the temperature rises 14 days before spontaneous menstruation, indicating that ovulation has occurred.

7. In 90 cycles we could compare the basal temperature curves and endometrial biopsies. Eighty-seven cases showed identical results with both methods.

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A case of Spontaneous Extra- and Intra-Peritoneal Rupture of a Hydronephrosis in Pregnancy

BY

I. Colin Campbell, M.B., M.R.C.S.,

Assistant Resident Surgical Officer, St. Mary's Hospitals, Manchester.

The following case is reported because of its rarity and because, so far, a similar one has not been found in the literature.

A woman, 37 years of age, in her third pregnancy, was admitted to St. Mary's Hospital, Manchester, one afternoon for investigation of the renal tract. She had haematuria, persistent for the last 2 months. About a year before she had had "kidney trouble" with pain in the right lumbar region lasting for 3 to 4 days. At that time there were no urinary symptoms. During the 3 months prior to admission, she had noticed a lump in her right side, which did not increase in size. For the last 2 months, there had been blood in her urine; this improved by rest in bed for a week. She had also had a dull aching pain in the right lumbar region occasionally passing down into the groin.

On admission her general condition was satisfactory, her colour was good, pulse-rate 68, blood-pressure 135/75 mm. Hg. The size of the uterus corresponded to the period of amenorrhoea (34 weeks) and the foetal heart-sounds were present.

In the right lumbar region there was a swelling, tender on pressure, difficult to define and considered possibly to be renal in origin. The other systems were normal. The laboratory findings at this time were:

Blood. Haemoglobin, 72 per cent; red-blood cells, 4,330,000; white-blood cells, 11,875; polymorphs, 26 per cent; mononuclears, 74 per cent; platelets, abundant; colour index, 0.85.

Blood urea. 31 mg./100 ml.

Blood group A (2)..

Urine. Numerous red-blood cells in wet film. Culture, sterile.

The patient's condition remained satisfactory until the following morning, when she vomited 3 times. The last attack, occurring about 7.30 a.m., was associated with a bout of coughing. Her general condition then deteriorated. She was pale, with sighing respiration, pulse 124, blood-pressure 80/60. foetal heart sounds were not audible.

Inspection of the abdomen showed a decrease in movement. On palpation it was now guarded, with deep tenderness in both flanks. The uterus was irritable. Percussion in the flanks showed the presence of shifting dullness. Rectal examination revealed that the foetal head was low in the cavity of the pelvis and that there was no tenderness in the Pouch of Douglas. There was no loss of blood *per vaginam.* A catheter specimen of urine obviously contained blood.

A provisional diagnosis was made of intra-abdominal haemorrhage, originating from a renal tumour, probably a hydronephrosis.

Mr. W. Thompson, F.R.C.S. (Resident Surgical Officer at the Manchester Royal Infirmary), confirmed this view and it was considered that a laparatomy was indicated.

A blood transfusion was commenced and the patient taken to the theatre (8.30 a.m.), after hypodermic morphia, gr. ¼; atropine, gr. 1/60.

A right upper paramedian incision was made. The abdomen contained 2 pints (1,200 ml.) of blood-stained fluid. A cystic swelling in the position of the right kidney, and a retroperitoneal haemorrhage were next observed. The left kidney was normal. The swelling was exposed by retracting the hepatic flexure of the colon downwards and the duodenum medially. Further dissection revealed a large hydronephrosis into which haemorrhage had taken place. The posterior parietal peritoneum was incised and the hydronephrotic sac was opened. A half-pint (300 ml.) of blood clot was evacuated. The kidney and sac were dissected free and

removed. Further blood loss was minimal. The abdomen was closed in layers after stitching the hole in the posterior peritoneum. A stab-drain was brought out in the right hypochondrium.

Total blood loss was estimated to be nearly 3½ pints (2 litres). Transfusion was continued until the administration of 4 pints (2,400 ml.) was completed.

Post-operative treatment.

This consisted of adequate sedation (morphia, gr. ⅙, 4-hourly, for 24 hours), gradual daily shortening of the drainage tube and the administration over a period of 24 hours of 4 pints of 20 per cent dextrose solution intravenously to provide fluid and to promote diuresis.

At 5.30 p.m. on the day following the operation, labour started and the membranes ruptured shortly afterwards. The patient delivered herself by natural forces of a stillborn macerated foetus weighing 4 pounds. The total time in labour was 1½ hours. From this event, until the end of her period in hospital, 21 days in all, the patient underwent a normal convalescence. Her condition on discharge was excellent.

ADDENDA.

Pathological Report. Hydronephrosis. Kidney measures 5 by 3 inches with a cystic cavity measuring 5 by 4 inches. Numerous haemorrhagic areas in wall of cyst and in substance of kidney.

Laboratory Reports.

Fifth day (post-operative) *Blood.* Haemoglobin, 62 per cent; red-blood cells, 3,310,000; colour, index, 0.95.

Twelfth day (post-operative). Blood urea, 30 mg. / 100ml.

The Use of a Hodge Pessary for Correcting Backward Displacement of the Uterus*

BY

T. N. A. JEFFCOATE, M.D., F.R.C.S., F.R.C.O.G.

Professor of Obstetrics and Gynaecology, University of Liverpool.

ALTHOUGH it is generally agreed that a mobile retroversion or retroflexion of the uterus is usually symptomless, its correction as a temporary measure is sometimes indicated for purposes of diagnosis, during early pregnancy or the puerperium and in cases of infertility, etc.

In such circumstances it is usually taught that the position of the uterus should be first corrected by bimanual manipulation as a temporary measure is sometimes volsellum, and that thereafter the position of the uterus should be maintained by inserting a pessary. The best pessary for this purpose is probably the Hodge, or one of its modifications; a ring is not so satisfactory but may have to be used if the retroversion is associated with prolapse or a defective perineum. However, reposition of the uterus by the accepted method is not so easy a procedure as it appears, and is as a rule beyond the capacity of anyone without special experience and training. Indeed, many gynaecologists often find it necessary to resort to general anaesthesia in order to perform the manoeuvre, especially in nulliparous women. The secret in any case is to manipulate the cervix rather than the body of the uterus itself. One of the difficulties is that the uterus is not always within easy reach, moreover it may return to its former

position when the operator removes his fingers to pick up the pessary for insertion.

It is now well established that in the comparatively rare cases in which an impacted retroverted gravid uterus does not correct itself spontaneously, and cannot be replaced, a useful procedure is to insert a large-size ring pessary, and the continuous pressure causes a gradual correction of the position of the uterus. The object of this note is to point out that in all cases, no matter whether the woman be pregnant or otherwise, the easiest way to correct retroversion or retroflexion is to do it with the pessary itself. The pessary, however, is used as a lever on the cervix and not as an agent for exerting pressure on the fundus as in the case of the impacted uterus mentioned above.

Procedure.

With the patient in the left lateral position and the uterus still retrodisplaced, a suitably sized Hodge pessary is inserted and allowed to take up its own position. It will be found that the upper rim naturally comes to lie in the anterior fornix, the lower bar projecting just beyond the introitus (Fig. 1). One or two fingers are then inserted behind the lower bar, through the pessary and in front of the upper rim. Pressure is exerted backwards on the upper end, which is pushed against the anterior aspect of the cervix (Fig. 2). If the upper end of the pessary is out of reach the fingers

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can be placed on anterior aspects of the side bars as high up as possible. With continued pressure the cervix is deflected backwards and the body of the uterus begins to rotate forwards. Ultimately the upper end of the pessary slips past the cervix into the posterior fornix and into its correct position (Fig. 3). By this time the retroversion is nearly always automatically corrected. Sometimes it is only partially corrected, the uterus lying with its axis vertical. In such cases the upper end of the pessary is pushed firmly against the posterior vaginal wall just behind the cervix, and the posterior fornix "stroked" backwards and slightly downwards with the pessary (Fig. 4). At the same time the lower end of the Hodge comes to lie at a higher level against the anterior vaginal wall. The cervix is thus levered further backwards, the fundus uteri comes forwards, and the pessary is at the same time left in its proper place.

There is a knack in carrying out the operation, but once it is learned the method is extremely simple and can be carried out without much experience. I have rarely known it to fail except when the uterus is fixed by adhesions; indeed, it can be employed as a test of mobility. Except in the case of virgins it is never necessary to administer an anaesthetic. The manoeuvre causes the patient such little disturbance that she does not realize that it has been carried out. One of the advantages of the technique is that it does not involve any pressure on the body of the uterus and it can be applied during early pregnancy, even in patients who habitually abort, without any risk of causing an abortion. Indeed, it is so easy, painless and safe that there is much to be said for using it as a routine when a retroverted gravid uterus has not corrected itself by the 8th or 10th week, rather than take the admittedly small risk that the uterus will become
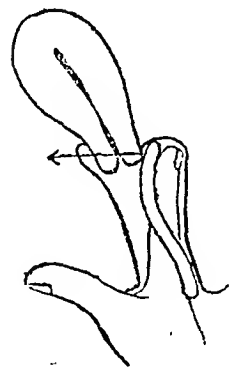
FIG. 1.   FIG. 2.

FIG. 1.
Insertion of Hodge pessary with uterus in position of retroversion. The upper end of the pessary comes to lie in the anterior fornix.

FIG. 2.
One (or two fingers) inserted through the pessary, the upper end of which is pressed firmly backwards against the cervix.
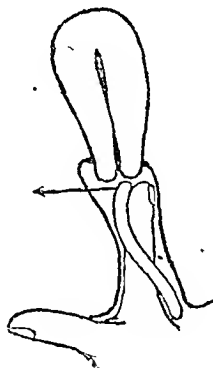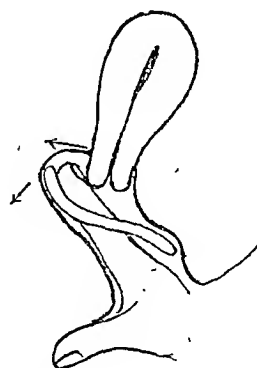

FIG. 3.   FIG. 4.

FIG. 3.
As cervix moves backwards and fundus begins to rotate forwards, the upper end of pessary slips behind the cervix into posterior fornix.

FIG. 4.
If uterus is not already in good position, anteversion is increased by pressing the upper end of pessary further backwards and slightly downwards. The cervix is thus pulled backwards by putting tension on the posterior vaginal wall and the overlying tissues.

impacted. The method is also useful in the puerperium, when tenderness of the vaginal walls and perineum may make the usual manipulation both difficult and painful. If the vaginal walls and perineum are atonic, however, a Hodge pessary may not be retained and a ring pessary is necessary. The same technique can be carried out with a ring, but it is perhaps not quite so efficient.

The manoeuvre whereby the pessary is slipped from the front to the back of the cervix as recommended here is by no means original. It is described in most textbooks, both new and old, as a standard procedure *after* manual replacement of the uterus. The suggestion here is that it should be carried out *before* replacing the uterus and as a means of replacement.

I

Pyrexia as a Sign of Endometriosis*

BY

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It is a well-established clinical observation, but one which in practice is sometimes overlooked, that the presence of free blood in the peritoneal cavity often causes a rise in temperature. Haematoperitoneum can give rise to a clinical picture not easily distinguished from septic peritonitis—pain, tenderness, distension, vomiting, ileus and pyrexia. Slight pyrexia is sometimes seen in cases of tubal abortion and pelvic haematocele and may lead to an error in diagnosis. The rise in temperature which is not uncommonly seen for 2 or 3 days after operation and which is labelled " reactionary " is probably due to some oozing of blood into the peritoneal cavity or into tissues at the site of operation. The "·reactionary " temperature is more noticeable and more prolonged when there has been much separation of adhesions or difficulty in achieving complete haemostasis.

Bearing in mind these considerations it might be expected that endometrioma, a condition in which haematoma formation is characteristic and in which blood cysts sometimes discharge their contents into the peritoneal cavity, could cause pyrexia. Such an association is not mentioned in textbook descriptions of endometriosis, yet it not only occurs, but is sufficiently frequent to be of practical importance.

My attention was first drawn to this point in 1939 when a doctor asked me to see his wife who, at the age of 33, was complaining of severe dysmenorrhoea, and during each period had noticed a rise in temperature up to 100°F., this being associated with a good deal of malaise. She had wide-spread pelvic endometriosis which required radical surgery, and after the operation she has remained well and free from menstrual pyrexia. Since that time 'all patients in whom endometriosis was suspected have been asked whether their temperature altered during menstruation. It has proved exceptionally difficult to get information on this question. Most women attribute their general malaise to the severe pain or to the period itself, and do not trouble to take their own temperature. Amongst the hospital class of patients in particular it is almost impossible to get any reliable evidence; private patients, however, tend to be rather more observant.

During the past ten years 120 cases diagnosed as pelvic endometriosis were seen in private practice, but the diagnosis was proved only in 91, the remainder being treated without operation. Among the 91 there were 10 cases in which the occurrence of pyrexia was a significant clinical feature' —noticed by the patients and recorded. In 2 of the 10 cases, however, operation revealed evidence of inflammatory appendage disease as well as pelvic endometriosis, and these are excluded. Among the remaining 8 there was no sign of infection either in the pelvic organs or elsewhere, and in all cases removal of the growth, or the major portion of it, was followed by complete resolution of the temperature; this

was permanent except in 2 cases where a return of pyrexia coincided with a recurrence of the growth. In one of these the activity of the tumour and menstruation itself was suppressed for 14 weeks by giving androgens. During this time the patient experienced neither pain nor pyrexia, but both returned when the treatment was suspended.

The degree of pyrexia was not gross in these cases, 101 to 102°F. being the highest noticed by the patients. Its occurrence too was variable; sometimes it was present intermittently throughout the menstrual cycle, but typically it occurred cyclically during menstruation, gradually disappearing during 1 or 2 days after the flow ceased.

It seems likely that pyrexia is a feature of active endometriosis more frequently than these figures suggest. The 91 cases include all types of case—uterine endometriosis, a growth which often does not menstruate, small patches of endometriosis occurring on an exposed surface such as the abdominal wall or perineum, and growths which were almost certainly functionless in that they were found incidentally during operations on post-menopausal women. Above all there remains the probability that menstrual pyrexia often passes unnoticed. In this connexion it should be pointed out that of the 8 patients who reported pyrexia, 4 were members of doctors' families and were under prolonged and expert observation.

Body temperature normally varies with the menstrual cycle, but the peak occurs pre-menstrually and the onset of the flow is characterized by a fall. A rise in temperature during each menstrual period should, therefore, be regarded as significant of some pathology. It may occur sometimes in pulmonary tuberculosis when the lesion appears to be more active during menstruation. It might presumably occur with genital tuberculosis, but in gonococcal or pyogenic salpingoöphoritis it would not be likely to continue for more than a few months at most. It might also be noticed in women who have retrograde menstruation. However, I can only recall one patient who had a long-standing menstrual pyrexia and in whom there was no evidence of pelvic endometriosis. She too was a doctor's wife, a young nulliparous woman who for nearly 2 years had a temperature of 99°F. with each period. Her husband had phthisis, but there was no evidence of this so far as she was concerned. No pelvic abnormality was found; she had no treatment, and after some time the menstrual pyrexia cleared up; she subsequently had children, and has remained well for 6 years since.

The importance of recognizing that pyrexia may be produced by endometriosis is in regard to the differential diagnosis between this condition and pelvic infection. This aspect is emphasized by the details of a recent hospital case (not included in the above).

The patient, E.H., was single, aged 26 and a nurse. She was admitted with a history of 2 weeks' lower abdominal pain associated with a temperature rising to 100–101°F. She had had dysmenorrhoea during the last 3 periods only, some intermenstrual yellow discharge and occasional slight intermenstrual bleeding. Eight years previously she had had an appendix abscess, necessitating 2 abdominal operations. On examination she was found to have a retroverted uterus with restricted mobility, and although neither appendage was palpably enlarged, both were acutely tender, especially the left. The urine was normal. A diagnosis of acute salpingitis was made, although there was no increase in blood sedimentation-rate and no leucocytosis. Treatment by rest in bed, hot vaginal douches, intrapelvic heat applied with Elliott's apparatus, sulphadiazine (35 g. in 5 days), penicillin (2 courses of 450,000 units and 2,200,000 units respectively), failed to have any dramatic effect. The pyrexia continued intermittently and attacks of pain recurred, although

the pelvic organs became rather less tender on examination. The highest temperature recorded was 102°F.; the pulse-rate varied between 80 and 130. Other investigations, X-ray of chest, blood-culture, bacteriological examination of faeces and urine, serum-agglutination tests, all gave negative results and ultimately it was decided to carry out laparotomy. This was done 7 weeks after admission when, after a remission, she had another attack of pain and the temperature began to rise again. No sign of inflammation was found in the lower abdomen or pelvis and not a single adhesion remained as a result of the appendix abscess. The genital organs were normal except for a patch of endometrioma on the surface of the left ovary. This was not more than 1 cm. in diameter and there were no adhesions to it. There was a little free blood in the pelvis which may have come from the surface of the growth, or may have escaped from the uterus along the Fallopian tubes. In either case it might have been precipitated by examination under anaesthesia prior to laparotomy. The affected area of ovary was resected and the diagnosis subsequently confirmed by microscopic examination. The patient's temperature was normal within 24 hours of operation and she remained apyrexial until her discharge from hospital 16 days after operation. She has remained well during the subsequent 6 months.

In this case there was not any sign of long-standing intra-pelvic haemorrhage at the time of operation, and there were no adhesions; the total area of growth was small and only minute blood cysts were present. Even so, it would appear that the endometrioma was sufficient, in a patient whose heat-regulating centre may have been unusually sensitive, to cause a considerable rise in temperature—and this in turn made the diagnosis difficult.

The occurrence of pyrexia in association with endometriosis is also mentioned by Holmes (1942). In his series of 80 proved cases its incidence was 8.7 per cent.

REFERENCE.

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Plastic Surgical Treatment of Congenital Transverse Diaphragms of the Vagina

BY

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One of the rare congenital anomalies of vaginal development is the transverse diaphragm. Rubin (1944) gives to this anomaly the name "cervical phimosis." There may be one or more partitions, the formation of which brings to mind the vagina of the ewe which bears transverse circular folds.

As Petsalis (1936) has proved, these congenital transverse diaphragms of the vagina are due to the incomplete dissolution of the epithelium which fills the Müllerian ducts during foetal life even after the coalescence at their caudal end. This incomplete dissolution may occur at one or more points, thus forming one or more occlusions. If only one of these exists it is usually found in the upper vagina. The diaphragms thus formed may bear one or more miniature openings either in the centre or the periphery, not differing histologically from the vaginal walls.

Provided there is an orifice in each of these partitions menstrual flow occurs regularly and no haematocolpos is formed. Diagnosis of this anomaly can, therefore, only be made after marriage as the congenital diaphragms completely conceal the cervix and thus hinder normal intercourse, fertility or delivery.

As soon as such a diagnosis is confirmed surgical treatment is indicated. The procedure adopted until quite recently was the circular excision of the diaphragm and suturing of the raw area. This operation caused a stenosis of the vagina in the form of a non-expanding ring at the place of the excised diaphragm. Dannreuther (1944) used the transverse incision of the occluding transverse membrane which however does not eliminate the disadvantages in as much as it does not give the vagina its normal size and perimeter.

In an effort to avoid any such disadvantages a modified Petsalis method was used with full success in the following case.

CASE REPORT.

V. M. D., aged 26, married 3 years, nullipara, menstrual flow normal, duration 3 to 4 days.

First examined on July 14th, 1944, complaining of dyspareunia with subsequent insomnia and neurasthenia. Bimanual examination revealed an obstruction preventing the introduction of the finger further than 2 inches inside the vagina. Upon inserting the Kristeller's vaginal retractor No. 2 as far as it could go a transverse diaphragm with a small opening in the centre, about 3 mm. diameter, was revealed. Rectal bimanual examination revealed a normal-sized retroverted uterus and normal adnexa.

On May 29th, 1945, an operation according to the Petsalis method was carried out as follows:

Using knife-handle No. 4, blade 22, the first radial incision (AB) was made, from the existing opening of the diaphragm to its base (Fig. 1). The result of this incision gave 2 triangular surfaces BAC and $BA'C$ (Fig. 2).

After picking up points A, A', B and C with Kocher forceps the sides BAC and $BA'C$ were undercut to a depth of 1 cm. with knife handle No. 4, blade 23, thus giving a diamond $BACA'$ (Fig. 3). Silk 3-o was passed and tied from point C to B of the diamond (Fig. 4) thus drawing the edges together to form a transverse line AA' (Fig. 5).
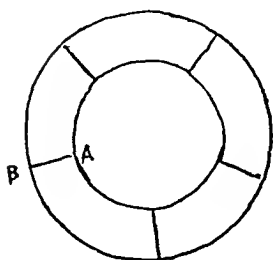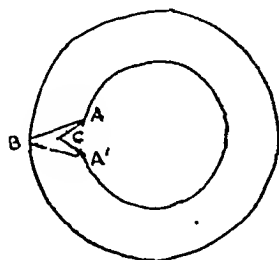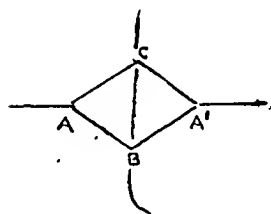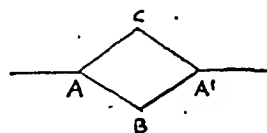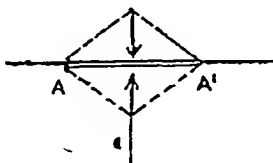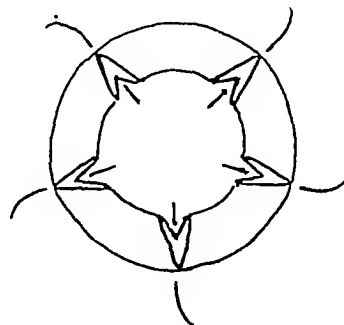
FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIG. 5.

FIG. 6.

(In order to show the method of incision and suture, the central perforation has been greatly exaggerated.   Diagram from Petsalis with slight alterations.)

The same procedure was carried out in all 5 incisions consecutively (Fig. 6).

The end of the operation revealed the hitherto concealed cervix. Then the whole vagina was painted with Mercurochrome solution, packed with gauze and left for 24 hours. The 9th day after the operation the silk sutures were removed and the patient was discharged on June 12th, 1945. She was asked to report a month later for examination.

She came on July 15th, 1945, and normal bimanual examination was easily made without any discomfort to the patient. The Kristeller's vaginal retractor No. 3 was easily inserted to the full depth of the vagina and the cervix was clearly observed. Distention, with both blades of the retractor, was accomplished without difficulty or causing pain. At the level of the operation 2 small atrophic folds were observed similar to *carunculae myrtiformes* in appearance.

The advantage of this surgical method is that the resulting transverse scars being parallel to the normal folds of the vagina do not hinder its dilatation at the site of the once existing diaphragm.

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LOUIS CARNAC RIVETT

Obituary

LOUIS CARNAC RIVETT

M.Chir., F.R.C.S., F.R.C.O.G.

LOUIS CARNAC RIVETT died in the Middlesex Hospital on 5th September, 1947, after a long illness borne with heroic gaiety and fortitude.

He was born in Stockport, Cheshire, in 1888, son of the high sheriff of Caernarvon. Educated privately and at Trinity College, Cambridge, he graduated B.A. in 1909, and continued his medical education at Middlesex Hospital, obtaining L.R.C.P., M.R.C.S. in 1912. He filled the posts successively of house surgeon, casualty surgical officer, and obstetric house surgeon, at Middlesex Hospital, and obtained the F.R.C.S. (Eng.) in 1915, and M.Chir. (Camb.) in 1916. His career in obstetrics and gynaecology was interrupted by service in the Army and R.F.C., Medical Branch. The end of the 1914–18 war saw him as surgeon in charge of the Anglo-French Hospital at Le Tréport. Returning to obstetrics and gynaecology he was appointed to the staff of Queen Charlotte's Hospital and the Chelsea Hospital for Women, the Royal Masonic Hospital, King George's Hospital, Ilford, and the Cottage Hospital, Welwyn. In 1930, on the retirement of Sir Comyns Berkeley, he joined the Honorary Staff of Middlesex Hospital.

He was examiner in his specialty for the Universities of Cambridge and Bristol and the Conjoint Board, and was part author of the *Queen Charlotte's Hospital Practice of Obstetrics* (1st edition, 1927) and *Sex Ethics* (1934). In addition he read many papers before the Royal Society of Medicine and the Hunterian Society, and was a regular attendant at the meetings of these bodies, when he nearly always had something to contribute of acumen and experience, salted with a pleasant dry humour. On the foundation in 1929 of the Royal College of Obstetricians and Gynaecologists he was made a foundation member and represented the members of the Council until 1936, when he was created F.R.C.O.G. He was editorial advisor to the Section of Obstetrics and Gynaecology of the Royal Society of Medicine, Honorary Secretary for some years of the Section of Obstetrics and Gynaecology of this society and Secretary of the National Birthday Trust.

This tells only part of his extraordinarily busy life, for he was on innumerable committees where his judgment, his tact and good humour made him invaluable. He found time to travel abroad and on two occasions visited the U.S.A.; on the second visit he was made an Honorary Member of the American Gynaecological Society.

Louis Rivett was an able and sympathetic clinician and an excellent teacher, but as a surgeon he was in the front rank. He carried his imperturbability into the

operating theatre, where he combined it with a high degree of manual dexterity that made his performances the wonder and delight of beholders from all over the world. Legend has it that he completed a subtotal hysterectomy in $7\frac{1}{2}$ minutes and a total in 10, and I have seen him do a classical Caesarean section in 17 minutes. Such celerity derived from his extraordinary technical skill, his careful preparation beforehand, his deep experience; considerations of showmanship came last. Rivett never seemed to be in a hurry; his many hospital and private patients, his great number of friends, his nursing staff, his medical subordinates, always found that he had time to stop and listen and wait until he had done what he could for them or simply spent a most pleasant time in their company. Generous, and hospitable and very kind, many of the younger generation of obstetricians and gynaecologists in London owe him encouragement and friendship and help in social and professional affairs.

For all his accessibility he was reserved and even shy, but his goodness and strength were never more manifest than in the last 18 months of his life, when the tragic deaths of his wife and his only son were followed by the knowledge of his own mortal disease, all met with admirable courage, and for his own condition a wryly amused interest in the surgical and other treatment to which he was submitted.

There has gone with him something gay and kind that we can ill spare, and the world of surgery is poor of a good citizen.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A special meeting of Council was held on Friday, 3rd October, 1947, at the College House, with the President, Mr. William Gilliatt, in the Chair.

The Honorary Fellowship of the College was conferred on Professor J. M. Munro Kerr, Professor C. G. Lowry, Sir Ewen J. Maclean and Sir William Fletcher Shaw.

The following were formally admitted by the President to Fellowship:

Gavin Stiell Brown.
Glyn Alexander Davies.
Gerald Patrick FitzGerald.
Alun Morris Johns.

Frederick Gallagher McGuinness.
Ronald McRobert.
Rufus Clifford Thomas.

To Membership:

Henry Bernard Bagshaw.
George Henry Bancroft-Livingston
Isabella Russell Bishop.
James Tweedie Swan Brown.
Gwendoline Eardley Cockrem.
James McDiarmid Corston.
George Archibald Craig.
Kenneth Joseph Robson Cuthbert.
George Laurence Daly.
Rudolf Walter Danziger.
Burjor Cavas Dastur.
Josephine Alice Davidson.
Norman Eric Corrigan de la Hunt.
William Powell Greenlie Dickson.
Ian Donald.
Ian Alexander Donaldson.
Sara Margaret Field-Richards.
Thomas Benedict FitzGerald.
Ian Tuke Fraser.
Alan Macpherson Giles.
Adam McMurtrie Graham.
Earle Francis Beattie Hamilton.
Arthur Jack Hardy.
Lois Edythe Hurter.

David Worsley James.
David Hugh Lees.
Max Lipsitz.
George Ian Louisson.
William Love.
Cecil John MacKinlay.
James Theodore Mair.
Parvati Malkani.
Eileen Cathcart Miller.
Wilfred George Mills.
Philip Rene Mitchell.
James Duncan Murdoch.
Mary Louise Neville.
Edwin Ronald Ormerod.
Horace Gordon Page.
Nancy Perry.
Elliott Elias Philipp.
John Geoffrey Pritchard.
Eric Rawlings.
Elizabeth Margaret Rose.
David Arnold Fletcher Shaw.
Denys John Neal Smith.
Robert Alexander Russell Taylor.
James Walker.

At the termination of the ordinary meeting of Council held on Saturday, 4th October, 1947, Mr. Humphrey G. E. Arthure, London, assumed the office of Honorary Secretary.

A meeting of Council was held in the College House on Saturday, 22nd November, 1947, with the President, Mr. William Gilliatt, in the Chair.

The Honorary Fellowship of the College was conferred on the Rt. Hon. Field-Marshal Jan Christiaan Smuts, P.C., C.M.

The following were formally admitted to Membership of the College:

Robert John McConnell Jamieson.
Joan Edith Warner Mackie.

Stephen Parlee (*absentia*).
Ada Sau Haan Wong (*absentia*).

The following candidates have satisfied the examiners for the Diploma in Obstetrics:

Kenneth George David Abbott.
Edward Anthony John Alment.
Gerald Joseph Amiel.
Geoffrey Anderton.
John Killen Armstrong.
William Constantine Astley.
Winifred Nora Backhouse.
Allin Barrington Backus.
Henrietta Elizabeth Banting.
Charles Patrick Bennett.
William Roy Bodenham.
Charles Christopher Bowley.
Michael Bruser.
Charles John Champ.
John Stanley L'Anson Chesshire.
Stanley Normal Cole.
John Colquhoun.
Janet Ellis Webster Copland.
Joseph Mary Gabriel Costello.
Herbert Henry Crabb.
Robert Crawford.
Reginald Comyn Cummin.
Dominick Vincent Cummins.
Nora Christine Curran.
Reginald Cutts.
Charles Henry De Boer.
Nagala Subhadra Devi.
Christopher John Dewhurst.
Luther William Darley Drabble.
William James Driscoll.
Victor Drosso.
John Geoffrey Dumoulin.
Alan Eckford.
Donald Fleming Edmiston.
Morris Seymour Ellensweig.
John Eskell.
Joseph Firth.
John Henry Fisher.
George Herbert Flack.
Harold Derek Freeth.
Herbert John Friend.
Robert William Grayburn.
Eric Glynn Hall.

Archibald Hanton.
Stephen Lonsdale Hetherington.
Noel Michael O'Connell Hewett.
Gilbert Edward Hicks.
Robert Hodgkinson.
Edmond Ivor Holloway.
David Rees Hughes.
Alexander Hunter.
Robert William Hutchinson.
Charles Gibson Irwin.
Saulat Begum Jahan.
Edwards William Jeyaratnam.
Arthur Joffe.
Frederick William Johnson.
Edward Parry Jones.
Edward Wynne Jones.
Robert Arthur Spink Keighley.
Peter Gilbert Scott Kennedy.
Robert Warton Kennon.
Peter Murray Kerr.
John Edwin Kerton.
Bernard Thomas Kieft.
Muriel Gladys King.
Gouri Kirtane.
William Herbert Laird.
Joseph Lewis Lawrence.
Robert Paterson Lawrie.
John Bateman Lawson.
James McLintock Lees.
Merrick Halden Lloyd.
Mary Love.
Hugh McColl.
Kathleen Anne McDonald.
Richmond McIntosh.
Muriel MacKenzie.
Alistair Gordon MacLeod.
James Crawford MacWilliams.
Arthur Stuart Majury.
Hugh Naylor Mansfield.
Annamma Mathan.
Timothy Kindersley Maurice.
Theodore David Fountain Money.
Ivy Mary Morgans.

Maurice Frank Morton.
William Henry Oesterlein.
Gopal Chandra Pattanayak.
Joseph Henry Patterson.
Peter Cecil Alexandre Posford.
Michael Bertram Quane.
Walter James Ramsay.
Edgar Brian Rayner.
Derek Homer Read.
Denis David Lloyd Rees.
Jocelyn Graham Reynolds.
Henry Roberts.
Paul Savile Robinson.
Eric Stanley Rogers.
Monica Helen Roper.
John Rushton.
Geoffrey Temple Rutherfoord.
Helen Samson.
Mary Aletta Saunders.
Peter Gerard Seed.

Elizabeth Sarah May Sherrard.
David William Shields.
Irene Mary Susan Sloper.
Leonard Smalley.
Alan Ambery Smith.
Edward Michael Southern.
Elizabeth Mary Stokes.
Alan Taylor.
Alexander Percy Walker.
John Watson.
Joyce Watson.
Annesley Eliardo Beresford de Courcy
    Wheeler.
Joel Wilbush.
Mary Llywela Williams.
Robert Burgess Wilson.
Christopher Harrington Forrester
    Wood.
Esme Maria Wren.
Ratcliffe Bowen Wright.

BOOK REVIEW

"Utero-tubal Insufflation." By I. C. RUBIN. With 159 Illustrations. The C. V. Mosby Company, 1947. 50s.

THIS is a volume that should be studied by every thinking and teaching gynaecologist, for it is the masterly contribution of a pioneer who began the scientific study of the problem of sterility more than 25 years ago.

Part I discusses the anatomy, pathology and physiology of the Fallopian tubes, drawing special attention to those details of clinical and therapeutic importance which provides food for thought or conjecture; for instance it is shown that the longitudinal folds of mucous membrane are slight and scanty at the isthmus whereas they are thick and multitudinous at the ampulla; and, again, that in the intramural portion of the Fallopian tube there is a sphincter-like action of the muscle at the ostium that undergoes alternate dilatation and contraction. This is of importance not only as regards a passage of gas, but far more so for the passing of the fertilized ovum, for, whereas the force of the non-pregnant uterine contractions is on an average only 0.3 to 0.5 mm. Hg. that of the Fallopian tubes is 30 to 40 mm. Hg. Moreover Dr. Rubin clearly demonstrates that this peristaltic tubal muscle-tone is greatest at the mid-cycle when the ovum must be hurried along the tube, but (and this is the point he drives home) in cases of hypoplasia, the stigmata of which every gynaecologist should know, where there is hypofunction of the ovaries, then the rate and amplitude of the tubal contractions, once any spasm has been countered by octyl nitrite or the like, are minimal. The problem of spasm comes in for much consideration. Admitting that it is most often associated with deranged metabolism, Dr. Rubin thinks that it is of the nature of pyloric spasm and is due to an overstimulated autonomic or an exhausted sympathetic nervous system. The use of various drugs for this condition is discussed. Chapter II is of particular interest to the clinician and demands close study. Dr. Rubin is convinced of the part played by appendicitis in the causation of sterility. His records, using insufflation, bear out those of others working with lipiodol, that not less than 15 per cent of both primary and secondary sterility cases give a history of acute appendicitis. Equally certain is he from his own records that induced abortion is responsible for at least 35 per cent of occluded tubes, the actual site of closure being more often at the intramural portion than in the rest of the tube length and therefore more intractable to surgery; although on this point, Dr. Rubin, like Mr. Victor Bonney, strikes an optimistic note, for he is sure that as technique improves and as more cases are tackled conscientiously and scientifically with the aid of penicillin and chemotherapy the results will greatly improve. For this view he gives chapter and verse and presents some beautiful drawings done at the time of laparotomy which he hopes will convince or help a rising generation of gynaecologists. Part II gives a very full account of the technique and readings of tubal insufflation which cannot fail to enthuse the neophyte even though at present on the English market, we have no apparatus as simple and foolproof as the American model he depicts. Part III deals with the therapeutic aspects of insufflation and this section is that which is perhaps of most guidance to the practising gynaecologist, for facts and figures and comparisons are detailed. It would appear that if one takes an average of all the cases (and they run into many thousands) that 18 per cent of women become pregnant within 2 months of insufflation and that a very definite added proportion become so after that period and / or after repeated insufflations. In this connexion it is interesting to read that out of 590 patients 41.8 per cent had initial gas-pressures above 100 mm. Hg., which may be taken as evidence of impaired patency and would indicate the probability or advisability of repeated blowing of the tubes. For this reason, if for no other, Dr. Rubin thinks the value of the kymograph cannot be overestimated. Another point that is stressed is the effect of contraceptive precautions upon the inci-

dence of immediate future conception. Rubin shows this quite clearly on p. 258 where he categorically asserts that in 50 per cent of those who became pregnant after insufflation there was an interval of at least 2 years before they did so. He states many young women to-day employ precautions only to find, to their surprise, after discontinuing the practice that they cannot become pregnant. He considers that the use of chemicals, pessaries, douches, etc., alter or disorganize for a longer or shorter time the cervical mucosa and bacterial flora of the vagina. Moreover, it is his opinion that the practice of *coitus interruptus* is attended by sequelae as yet not understood which may have a deleterious influence on the mechanism of conception. Assuredly these are weighty words from such an authority.

Part IV surveys the 2 methods of investigation commonly used, namely insufflation and lipiodolography. It is agreeable to find that the author does not condemn oil or viscorayopaque injections although his own views, as he says, have been biased by the fact that in a series of very nearly 10,000 cases there is a record of 17 subsequent pelvic infections, a thing that he states cannot occur after air or gas, a statement that not all would agree with. The probability of accident, he remarks, depends much upon the judgment and skill of the operator. There is little doubt in Dr. Rubin's mind that from a therapeutic and surgico-strategic point of view the technique of hysterosalpingography has to be mastered; moreover for the determination of faults in the development of the Müllerian tract which may be causes of abortion there can be no question of its importance to the surgeon. Finally, for those who may hesitate to purchase this masterpiece, it is perhaps worth recording that out of 41,094 patients who were insufflated, the tubes were patent in 58 per cent, non-patent in 30 per cent, partially patent in 7 per cent, and spasmodic in 5 per cent. The reviewer well remembers the crowded meeting at the Royal Society of Medicine in 1925 when Dr. Rubin first demonstrated his method to an audience in this country and gladly recalls the enthusiasm with which he was greeted. This book is indeed a worthy monument to a life's work.

V. B. GREEN-ARMYTAGE

REVIEWS OF HOSPITAL REPORTS

MEDICAL REPORT OF THE GLASGOW ROYAL MATERNITY AND WOMEN'S HOSPITAL FOR THE YEAR 1945.

This hospital contains 174 beds—73 antenatal, 75 postnatal, 15 for cases of abortion and 11 for patients who require to be isolated. Among 3,933 admissions 2,772 deliveries occurred. Seventy per cent of the cases admitted were considered to be abnormal. This is attributed to the high incidence of malnutrition, overcrowding and rickets in the area served by the hospital. There were 488 cases of abortion. There is also a large outdoor service through which 2,051 women were attended in their own homes where the infants numbered 2,014.

Maternal death occurred in the hospital on 34 occasions (0.86 per cent or 13.32 per 1,000 live-births). Full details of each death are given under the categories, intercurrent diseases 7, complications of pregnancy 8, complications of delivery 13 and complications of the puerperium 6. In the report of a large hospital such as this information of value is to be found whatever the obstetrical interest of the reader. But all obstetricians must find the study of maternal death particularly instructive. From the 10-year survey in the appendix we learn that this figure of 34 is the lowest during that time. Some of these deaths were unavoidable, others were really avoidable but occurred for reasons beyond the control of the hospital; while others—can any large hospital dealing constantly with serious cases claim never to have an avoidable death?

In 4 of the 7 fatalities due to intercurrent diseases congestive heart failure was the responsible factor. To reduce deaths from this cause not only is close co-operation between general practitioner, antenatal clinic medical officer, obstetrician and physician necessary, but instruction of the patient is important. One of these patients had had to spend 2 months in bed prior to delivery in her previous pregnancy. After that she was discharged home "reasonably well". Was she given contraceptive advice or asked to consider being sterilized? Another was treated by her own doctor for "chronic bronchitis and asthma" during the pregnancy and was admitted moribund. How many patients suffering from mitral stenosis, who become pregnant, are told how serious the common cold may be for them, and what to do if they develop a cold? How great the teacher's responsibility!

Among the 8 fatalities classified as complications of pregnancy 6 had eclampsia and 1 concealed accidental haemorrhage. It could not be claimed from the details provided that any one of these was a case of fulminating eclampsia without some warning manifestation. It may be that the riddle of toxaemia must be solved in the laboratory, but in the meantime the teacher must tirelessly reiterate the importance of early diagnosis and the necessity for proper supervision when the diagnosis has been made. The responsible authorities, too, must provide adequate beds for the treatment of these patients—one patient with hypertension (150/100), albuminuria and oedema had to be sent home as a bed was not available.

Of 13 fatal complications of delivery postpartum haemorrhage was a principal factor in 7. Haemorrhage is now the principal cause of maternal death. The treatment of antepartum haemorrhage is fairly satisfactory nowadays. But this cannot be said about postpartum haemorrhage. It is impressed upon the medical student that he must know exactly what to do when confronted with a case of postpartum haemorrhage. Yet even experienced obstetricians differ about its treatment. Midwives attend most of the confinements in this country; but at a recent meeting of the Royal Society of Medicine devoted to this very subject there was uncertainty about what the midwife

should be taught to do when she meets with post-partum haemorrhage. This subject requires further serious consideration.

Of 6 fatal complications of the puerperium, sepsis was a principal factor in 4 (due in one case to perforation of the uterine wall during forceps delivery before admission).

After studying the details of the fatal cases which occurred during the year in this great hospital, the reader must agree that obstetricians have no grounds for complacency in spite of the falling maternal death-rate in the country. There is still ground for much improvement in our practice before we speak of an irreducible minimum in connexion with maternal death.

ANNUAL REPORT OF THE DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY OF THE BELLEVUE HOSPITAL, NEW YORK, 1945-1946

This report covers the period 1st June, 1945, to 31st May, 1946. It consists of 30 large pages of duplicated typescript stapled together. It is on the whole a catalogue of numbers of various presentations, antepartum complications, complications of labour, operations performed and the like in the obstetric portion of the report, followed by a similar long list of numbers of various pathological lesions encountered and operations performed in the gynaecological section. Any attempt at a critical survey of trends or practices in the hospital is completely lacking.

There were 2 maternal deaths among 1,538 deliveries. One of these was attributed to acute bacterial endocarditis, while the patient in the other fatal case showed severe hypertension and had a generalized convulsive seizure during delivery. Single case data are not provided for any obstetrical condition. Yet each maternal death is described at great length—1,200 and 1,300 words respectively. These descriptions are verbose, badly constructed and bristling with hospital slang. They make tedious reading at the end of a rather unimaginative catalogue.

The report shows that a considerable amount of good work is done in the hospital, but it is difficult to imagine that obstetricians from other hospitals will find it either of much interest or instructive.

THE MATERNITY UNIT REPORT, St. LUKE'S HOSPITAL (SURREY COUNTY COUNCIL), GUILDFORD, FOR THE YEAR 1946

In the short preface the reader is informed that the presentation of a comprehensive annual report for 1946 is made to mark the first post-war year and also to record a most successful year for the Unit. This new venture—that at least is the impression given—is surely a praiseworthy method of celebration.

The number of patients admitted to the Unit was 1,389 (total admissions 1,694) of whom 1,332 were delivered there. There was only 1 maternal death (0.08 per cent). There were 31 stillbirths (2.3 per cent), and infant deaths in the first 10 days numbered 27 (2.05 per cent).

The importance of the early recognition of toxaemia of pregnancy with early hospitalization is emphasized. There were 194 admissions among 138 booked cases in which toxaemia was observed, These patients gave birth to 140 infants of which 5 were stillborn and 2 died—a combined foetal mortality of 5 per cent. Among 20 emergency cases the foetal mortality was 10 per cent. In this hospital all cases which show a blood-pressure above 130/80 mm. Hg are considered to be toxaemic and are advised to go into the hospital for rest and investigation. Of course the lower the standard of hypertension is, the more likely is the foetal result to be satisfactory.

The report has been compiled with care and reflects the high standard of the work done in the Unit. The results achieved must be gratifying to the Staff. Nevertheless, certain modifications might make it of more interest to the reader. The preface of some 120 words might be expanded into a more interesting critical survey of the practice and achievements of the Unit. Certain clinics are held outside the hospital and are said to have been a success. More information might be given about these and about the antenatal hostel provided for patients who live in outlying villages and townships. The definition of what constitutes an " emergency " admission is far from clear. Maternal deaths should always be set out prominently with a paragraph about each one. A considerable search was necessary before the reviewer discovered that the one maternal death had occurred from obstetric shock following

Caesarean section for contracted pelvis in a booked case.

In the paediatric section single case data are given of all infant deaths and stillbirths in addition to a statistical summary. It is interesting to note that of 1,289 infants discharged alive, 1,074 were entirely breast fed on leaving the hospital.

REPORT OF THE PENINSULAR MATERNITY HOSPITAL, CAPE TOWN, FOR THE YEAR 1946

The report, which runs to 38 pages, opens with a critical survey of 15 pages embodying the salient features of work done in the hospital during the year. Three further pages are devoted to details of 5 cases of special interest. Then follows a statistical summary, which is succeeded in turn by tables for transverse lie, breech delivery, destructive operations, forceps delivery, primary uterine inertia, surgical induction of labour, antepartum haemorrhage, eclampsia, indications for Caesarean section, morbidity, maternal mortality, stillbirths and neonatal deaths.

The hospital is overcrowded. Into its 40 beds, 1,901 patients were admitted, and of these 1,663 were delivered in the hospital. Because of shortage of beds it was necessary to refuse admission to some 80 patients, most of whom suffered from some complication of pregnancy, but some were actually in labour. The morbidity rate (B.M.A. standard) was 5.7 per cent, and the overcrowding is considered an attributable factor. As many as 57 patients have been accommodated at one time—that is 42 per cent above capacity.

Certain differences appear between the European and non-European patients. The general incidence of syphilis is high (11.5 per cent), but the incidence among Europeans was 1.7 per cent, while among the non-Europeans it was 14.5 per cent. The Europeans showed a higher incidence of uterine inertia, and pre-eclamptic toxaemia was twice as common in them as in non-Europeans. In spite of the fact that syphilis accounted for 16.1 per cent of the neonatal deaths and that the incidence of prematurity was definitely higher in the non-European section, the incidence of neonatal deaths was slightly higher in the European section.

In reading the tables of individual conditions giving single case data, it will at once be evident that these differ in certain respects from similar tables to those annual reports which follow more closely the form suggested by the sub-committee appointed by the Council of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine (Proc. Roy. Soc. Med., 21, 1533–1542, 1928). At the head of each table is a short summary which should be read in conjunction with the paragraph referring to that condition, disorder or operation in the critical survey earlier in the report. At first glance one might think that in the single case data every case of the disorder or operation had been tabulated. But this is not so. There were 12 cases of transverse lie: 10 of these are set out in considerable detail, but 2 do not appear in the table. Similarly, there were 14 cases of eclampsia: details of 11 are given. The reason for this selection is not stated. Not all pathological conditions and major operations receive this selective single case treatment, e.g., in the antepartum haemorrhage table details are not given of any single case. The reason for this further element of selection is not indicated.

Where single case data are given they are extensive. Most of the details appear in " notes " or " remarks " at the end of a series of columns giving parity, maturity, etc. Yet in the welter of detail given there are surprising omissions, as will be found in the table of Destructive Operations (page 26). The last case is that of a 2-para (initials S. S.) for whom the 6th August was evidently an important date (presumably either the date of her admission or operation), craniotomy was performed for disproportion, but the patient's age is not given. The case immediately above that in the same table, a 12-para, whose age is also omitted, had a difficult craniotomy performed for maternal distress; but whether or not the foetus had died before the craniotomy was performed is not mentioned.

There were 4 maternal deaths (0.178 per cent). Eclampsia was the primary cause in 2, sepsis following Caesarean section in 1, while the last—a case of postpartum haemorrhage—died 45 minutes after admission in a moribund condition. In the critical survey it is not stated whether the hospital caters for the treatment of emergency postpartum haemorrhage in the patient's own home.

The report is so attractively printed that the reading of it is a pleasure.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts of articles which, though not of sufficient general interest for publication in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages, and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of thirty shillings per thousand words.

INDEX

ANATOMY

852. The Fibrous Nature of the Human Cervix, and its Relation to the Isthmic Segment in Gravid and Nongravid Uteri.

By D. N. DANFORTH. *Amer. J. Obstet. Gynec.,* 53, 541–560, Apr. 1947. 11 figs., 14 refs.

Aschoff, in 1905, defined the isthmus uteri in the non-pregnant uterus as the area lying between the histological and the anatomical internal os. The histological internal os marks the transition point from endocervical to isthmic mucosa, while the anatomical internal os 6 to 10 mm. above it is a constriction in the uterine lumen, marking the lower boundary of the corpus uteri. The mucous membrane of the isthmus is similar to that of the corpus but thinner, and richer in supporting tissue, while its glands are sparser and less sensitive to the ovarian hormones, and are said to be glycogen-free. The classical conception of the isthmus in pregnancy is summarized by Danforth as follows: " During the third month the isthmus elongates to about three times its former length, and this elongation is said to be accompanied by proportionate thinning. During the subsequent weeks ' unfolding ' occurs, so that the entire isthmus is incorporated into the formation of the ovum chamber; the uterine cavity then consists of cavum corporis plus the widened isthmic canal. The isthmus is now referred to as the lower uterine segment."

Danforth examined pregnant and non-pregnant uteri by Masson's trichrome stain (iron haematoxylin; acid fuchsin; aniline blue) to distinguish smooth muscle from fibrous tissue. His results were as follows. The basic structure of the cervix was found to be fibrous tissue with comparatively little muscle. In many specimens virtually no muscle could be found. In others there was as much as 40 to 45 per cent, but usually it did not exceed 10 or 15 per cent, and was scattered at random throughout the substance of the cervix. It seemed unlikely that the muscle could exert any sphincteric action. The amount of elastic tissue was insignificant, and it was most abundant around the walls of the larger vessels. The tissue above the cervix is composed predominantly of muscle, the transition occurring more or less abruptly at the level of the histological internal os.

During early pregnancy it was found that the length of the cervix does not change appreciably, while the elongation of the isthmus is proportional to that which occurs elsewhere in the muscularis of the uterus. There was no evidence of thinning of the isthmus before unfolding, but it is possible that it takes place later. Unfolding or dilatation of the isthmus occurs down to the region of the fibro-muscular junction, and after it has taken place no evidence remains of the anatomical internal os either macroscopically or microscopically. The unfolding of the isthmus seems to coincide with the time when the ovum completely fills the uterine cavity and thus requires more space for its accommodation. Because of these findings it is suggested that the uterus should be regarded as consisting of two parts, cervix and corpus, according to whether the fundamental tissue is chiefly fibrous or chiefly muscular, and that the isthmus uteri be recognized as a part of the corpus just as the fundus is part of the corpus. These observations help us to understand why the cervix is refractory to the stimuli which in the same organ give rise to such tremendous growth and contractile responses, and also the nature of the barrier that retains the products of conception within the uterus until their maturity. A rational explanation is also offered for the limitation of the unfolding of the isthmus at the cervico-isthmic junction.

F. J. Browne

853. A Study of the Surgical Anatomy of the Vagina, with Special Reference to Vaginal Operations.

By W. SHAW. *Brit. med. J.,* 1, 477–482, Apr. 12, 1947. 6 figs., 12 refs.

The surgical anatomy of the vagina is described in detail and new names are suggested for several sulci and folds which are of importance in relation to operative procedures on the vagina. The *paramenatal recess* is the term used for the small depression on either side of the urethra. About ¼ in. (0.6 cm.) below the urethral meatus there is a groove, the *submeatal sulcus*, often clearly defined when the anterior vaginal wall is prolapsed; it can be displayed by drawing down the cervix with a volsellum. This groove indicates the posterior margin of the urogenital diaphragm. A second groove, the *transverse sulcus of the anterior vaginal wall*, representing the approximate junction of the urethra with the bladder, can be defined about 1½ in. (3.75 cm.) from the urethral meatus. Further down the anterior vaginal wall there is a third groove, the *bladder sulcus*, denoting the lower limit of the bladder. Between the lateral vaginal and submeatal sulci there is a fold of skin termed the *oblique vaginal fold*; below and lateral to this fold there is a small recess—the *paraurethral recess*.

Methods of demonstrating the fascial layers deep to the vagina are described in detail. Attached to the anterior vaginal wall is a well-defined layer of fascia, the *vaginal fascia*, while a much thinner layer of fibromuscular tissue, the *vesical fascia*, covers the bladder. The *vesico-vaginal space* lies between these two layers of fascia. At the level of the transverse vaginal sulcus these two fascial layers fuse and pass downwards to become attached to the margin of the urogenital diaphragm at the submeatal sulcus. The vesical fascia is continued upwards on to the supravaginal portion of the cervix and is now termed the *vesico-cervical ligament*. The bladder septum which passes from the vesical fascia to the fascia covering the cervix lies on either side of the vesico-cervical ligament. The

chief function of the fused vaginal and vesical fasciae, which pass between the transverse vaginal sulcus and the urogenital diaphragm, is to support the urethra, and the term *post-urethral ligament* is suggested for this fascial band. Its upper cranial margin is usually well defined and gives rise to the transverse vaginal sulcus. The post-urethral ligament is attached laterally to the pubic ramus as far as the junction with the ramus of the ischium, and in the mid-line it is adherent to the bladder for a short distance upwards towards the cervix. As the nomenclature of the fascial tissues of the pelvis is confusing, it is suggested that the term *pelvic fascia* should be restricted to the dense fascial tissues covering the levator ani and obturator internus muscles, while the term *endopelvic fascia* is used for all other fascial layers.

The technique of anterior colporrhaphy based on the identification of the different ligaments and fascial layers is described. It is considered that, between the transverse vaginal and bladder sulci, the only direct supports of the bladder are the vesical and vaginal fasciae along with the anterior vaginal wall. Therefore in order to prevent any recurrence of cystocele it is essential to suture the post-urethral ligament, after mobilization of the bladder, to the front of the uterus at the level of the utero-vesical pouch. Stress incontinence can be overcome by a series of interrupted Lembert sutures through the post-urethral ligament, forming a shelf so that the urethra is stretched and elongated upwards and backwards. An essential feature in the author's operative technique for vaginal hysterectomy, described in detail, is to form a shelf incorporating the post-urethral ligament to support the bladder after the uterus has been removed. The first suture passes through the cut vaginal wall 1½ in. (3.75 cm.) from the urethra, through the post-urethral ligament and the cut edge of the peritoneum near its attachment to the bladder, then through the post-urethral ligament again and the vaginal wall on the other side. The first suture is reinforced by a second through the vaginal wall on one side, the post-urethral ligament, and the tissues at the upper end of the broad ligament (the ovarian ligament, Fallopian tube and round ligament) on either side, then again through the post-urethral ligament and the vaginal wall on the other side, so as to anchor the shelf formed by approximation of the upper portions of the broad ligament to the post-urethral ligament. It is also essential in this operation to remove as much peritoneum as possible from the pouch of Douglas; redundancy of peritoneum can be exposed by traction on the uterus delivered through the utero-vesical pouch. The subsequent development of a hernia of the pouch of Douglas after vaginal hysterectomy can be obviated while carrying out a colpoperineorrhaphy by suture of the utero-sacral ligaments, the rectal septa which represent the downward continuation of the utero-sacral ligaments, and even the two levator ani muscles to the posterior part of the shelf formed by approximation of the posterior portion of the broad ligament. This procedure, however, narrows and shortens the vagina and is not applicable to all cases. If normal coitus is to be resumed the utero-sacral ligaments only are sutured after removal of the peritoneal pouch. The importance of suturing the levator ani muscles at least 2 in. (5 cm.) above the level of the vaginal orifice is emphasized.

To control stress incontinence of urine associated with cystocele and prolapse of the uterus and urethra it is important to suture the post-urethral ligament in such a way that it is stretched in a sagittal direction. This suture may be reinforced by a series of reefing sutures on each side of the urethra. Stress incontinence not associated with prolapse can be controlled by suturing the upper edge of the post-urethral ligament to the front of the cervix or by means of a series of interrupted sutures fixing the post-urethral ligament to the vaginal wall at a higher level than normal.

T. N. MacGregor

854. **Our Study of Vaginal Cytology.** (Nosso estudo sobre a colpocitologia.)

By A. BITTENCOURT DE OLIVEIRA. *Brasil-med.* 61, 165–167, Apr. 19 and 26, 1947. 5 figs., 4 refs.

PHYSIOLOGY

855. **The Endocrine Function of the Uterus.** (A função endócrina do útero.)

By J. SIMOES E. SILVA. *Rev. Ginec. Obstet.*, 1, 371–383. Apr. 1947. 27 refs.

856. **Capillary Fragility and Menses in Rheumatic Girls.**

By E. E. BROWN and V. P. WASSON. *J. Pediat.* 30, 455–458, Apr. 1947. 23 refs.

This paper discusses the menstrual cycle and capillary resistance in 28 ambulant rheumatic girls. It is noted first that values for capillary resistance vary with season and age, and that capillary resistance is low in streptococcal infection, measles, and pneumonia; at the same time the menses may be excessive or early in onset. The average age in this group of patients was 13.4 years, and capillary resistance was 17.4 cm. of mercury as compared with 27 cm. in non-rheumatic subjects. The onset of the menstrual cycle tended to be early in the group (11.9 years as contrasted with 13.5 years for American girls); bleeding lasted longer and was more frequent. Capillary resistance was markedly high in autumn as compared with February, March, and April. The work rules out the likelihood of vitamin-C deficiency being the cause of this, and suggests that a more likely cause is variation in streptococcal toxin. Rheumatic fever is common in the autumn, but the peak of both streptococcal and rheumatic activity is reached in the spring.

Beryl Twyman

857. A Quantitative Determination of the Content of Contractive Substances in Human Sperm and their Significance for the Motility and Vitality of the Spermatozoa. [In English.]

By J. ASPLUND. *Acta physiol. scand.*, **13**, 103–108, Feb. 1947. 2 figs., 8 refs.

The depressor and plain-muscle-stimulating effects of sperm are attributed to factors such as prostaglandin and choline. The author has attempted to estimate the total amount of these substances in 155 specimens of sperm plasma, using rabbit gut and a standard prostaglandin solution prepared by von Euler's method. The substance or group of substances causing plain-muscle contraction was present in all specimens but the amount varied considerably. Some specimens caused a rapid tetanic increase in tonus unlike the typical prostaglandin curve. This effect persists after atropine and is due to some factor other than prostaglandin or choline. The amount of these substances present is not related to the life and motility of the spermatozoa.

                                        E. F. McCarthy

858. The Time of Ovulation.

By J. I. BREWER and H. O. JONES. *Amer. J. Obstet. Gynec.*, **33**, 637–644, Apr. 1947. 4 figs., 13 refs.

The authors have determined the time of ovulation by estimating the age of corpora lutea histologically. They agreed with Corner that reasonably accurate age calculations can be made by this means, though an error of 2 days in calculated age is considered reasonable.

The material was obtained from 100 women in active menstrual life. All had menstrual cycles within the limits established for normal. In most cases some pelvic pathology was present but in no instance had it disturbed the menstrual rhythm. The patients were unselected and no effort was made to operate at any particular time in the cycle. The material consisted of entire or resected portions of one or both ovaries and endometrium. Great care was taken to ensure that menstrual dates were accurately recorded, and, following the usual custom, the first day of bleeding was counted as the first day of the cycle. Operation was carried out on at least 1 woman on each day of the cycle except the third and twenty-seventh days. It was shown that 54 of the 100 patients had ovulated during the cycle studied, and the range of time of ovulation was from the eighth to the nineteenth days. There was a greater tendency to ovulate early than late, for only 1 patient ovulated after the seventeenth day and more ovulated on days 8, 9, 10, and 11 than on days 16, 17, 18, and 19. Of the 54 women who ovulated, 36 did so on days 12, 13, 14, and 15, with the highest peak on the fourteenth day.

Study of the endometrium of 1 woman ovulating early in the cycle showed it to be developed to a degree consistent with the age of the corpus luteum, and the authors suggest that the cycle concerned would have been shorter than the usual 28 days reported by the patient. The woman, ovulating on the nineteenth day also gave a history of 28-day cycles, but in fact this cycle was lengthened. One patient with 21- to 37-day cycles was operated upon on the fifteenth day and found to have a 5-day-old corpus luteum. Of the 46 women without evidence of ovulation, 10 were at the thirteenth or fourteenth day of the cycle. All except 1 had mature follicules. The exception was a woman of 48 years of age, neither mature follicle nor recent corpus luteum was found and the endometrium showed little evidence of stimulation. This was the only case in which failure of ovulation was strongly indicated. Four patients who had not ovulated by the eighteenth day had follicles suggestive of imminent ovulation.

The authors correlate their findings with ovulation time studies carried out by other workers by means of endometrial, ovarian, and early embryo histology (Rock and Hertig), study of unfertilized ova (Allen *et al.*), rectal palpation in the rhesus monkey (Hartman), human rectal (Gruelich *et al.*) and oral (Davis) temperature records, observations on cervical mucus (Lamar *et al.*), vaginal smears (Papanicolaou), and pregnandiol urinary excretion (Venning and Browne). The consensus is that ovulation usually takes place in mid-cycle with a range from the eighth to nineteenth day in patients with a 26- to 30-day cycle. In the discussion following this paper, Davis provided proof that the rise in temperature during the second half of the cycle is due to progesterone.

                                        Doreen Daley

859. The Genito-Pituitary Reflex and Ovulation. (Le réflex génitohypophysaire et l'ovulation.)

By R. SEGOND. *Presse méd.*, **55**, 359–360, May 31, 1947.

860. Observations on the Mechanism of Ovulation in the Frog, Hen and Rabbit.

By S. H. KRAUS. *West J. Surg.*, **55**, 424–437, Aug. 1947. 16 figs., 22 refs.

861. Electrical Detection of Ovulation. (La détection électrique de l'ovulation.)

By J. VARANGOT, S. VASSEY and M. COLLIARD. *Sem. Hôp. Paris*, **23**, 1350–1356, May 28, 1947. 5 figs., 32 refs.

862. Functional Uterine Haemorrhages. (Les hémorragies utérines fonctionnelles.)

By J. L. WODON and R. CORDIER. *Brux. méd.*, **27**, 1333–1342, June 15, 1947. 12 refs.

863. Skin Manifestations of Menstruation.

By K. WIENER. *Wisconsin med. J.*, **46**, 694–696, July 1947.

864. **Studies on Endometrial Alkaline Phosphatase during the Human Menstrual Cycle and in the Hormone-treated Monkey.**

By W. B. ATKINSON and E. T. ENGLE. *Endocrinology*, 40, 327–333, May, 1947. 5 figs., 7 refs.

PREGNANCY

865. **The Problem of Fertilization.**

By LORD ROTHSCHILD. *Brit. med. J.*, 2, 239–242, Aug. 16, 1947. 31 refs.

866. **The Anatomical and Biological Conception of Pregnancy.** (Concepto anátomo-biológico de la gestación.)

By E. GIL VERNET. *An. Med. Cirurg.*, 21, 361–374, June 1947. 10 figs.

867. **The Effects of Pregnancy and Relaxin on the Histology of the Pubic Symphysis in the Mouse.**

By K. HALL. *J. Endocrinol*, 5, 174–182, July 1947. 15 figs., 7 refs.

868. **Course of Pregnancy and Parturition in Women Treated for Primary Sterility.** (Sul comportamento della gravidanza e del parto in donne trattate per sterilità primitiva.)

By E. ROBECCHI. *Minerva Chir.*, 2, 296–299, Aug. 1947.

869. **A Study of Fetal Movements in Relation to the Mother's Activity.**

By D. B. HARRIS and E. S. HARRIS. *Human Biol.*, 18, 221–237, Dec. 1946. 1 fig., 8 refs.

The authors have studied foetal movements in relation to the mother's activity. They review the literature on the subject and contribute the results of their own investigations. Hicks, in 1880, first devised a pneumatic tambour to record such movements, and various types of pneumatic apparatus have been tried subsequently. Kellog, in 1941, used a mechanical device, consisting of metal abdominal plates and vertical rods, which recorded movements on a kymograph drum. Studies of foetal movement, based upon the mother's own observations, were made by other authors by the same method. Sontag and Richards observed the foetal heart rate at ten-beat intervals.

The object of the present investigation was to decide whether a 30-minute subjective observation would yield a statistically reliable measure of foetal activity; whether there was any relation between fatigue experienced by the mother and the amount of foetal activity; what relation there was, if any, between hour-of-day and day-of-week foetal activity, on the assumption that the hour of day or the day of the week might systematically affect the mother's activity; and what relationship the length of the mother's day and the number of hours she spent in bed had to the amount of foetal activity. All observations were made by the mother herself, who recorded foetal movements of varying degrees with a prearranged series of marks on a piece of paper during 30-minute periods.

It would appear that the mother's recordings of foetal activity furnished an accurate estimate. Movements increased in strength and number most rapidly during the first month of perceived motility, and the foetus was consistently more active at the close of the observer's day; but there was no constancy in the relative number of movements noted during morning or night. The evidence concerning the effect of fatigue on foetal activity is inconclusive.

870. **Maternal and Foetal Relations.** (Relaciones materno fetales.)

By M. GARRIGA ROCA. *An. Med. Cirug.*, 21, 298–310, May, 1947.

871. **Obstetrics and Cholinergy.** (Obstétrique et Cholinergie.)

By H. LABORIT and P. MORAND. *Gynéc. Obstét.* 46, 298–302, 1947. 3 refs.

872. **Placental Metabolism of Vitamin C. I. Normal Placental Content.**

By A. C. BARNES. *Amer. J. Obstet. Gynec.*, 53, 645–649, Apr. 1947. 12 refs.

Studies of maternal and foetal whole blood showed that the vitamin-C content was consistently higher in the foetal blood. Maternal venous whole-blood levels ranged from 0.29 mg. to 1.8 mg. per 100 ml. Foetal cord blood levels ranged from 1.2 to 2.48 mg. per 100 ml. and were always greater than those in the corresponding maternal blood. Placental levels ranged from 4.7 to 21.0 mg. per 100 g. of tissue with a mean of 9.4. In each of the 84 cases examined the placental level was considerably higher than either of the blood levels involved, ranging from 3 to 10 times the foetal blood content. A possible explanation of this high level in the placenta is that the placenta synthesizes vitamin C. A series of *in vitro* experiments ruled this explanation out. These results tend to support the postulate that the difference between the foetal and maternal blood level arises from a selective retention of ascorbic acid at the placental barrier. Further experiment showed that no such retention and storage occurs of carotene or thiamine.

F. J. Browne

873. **The Amniotic Duct as the Key Structure in the Determination of the Direction of Growth of the Human Placenta and its Orientation in the Uterus.**

By J. KRAFKA and L. BOWLES. *Amer. J. Obstet.* 53, 561–568, Apr. 1947. 11 figs., 11 refs.

It has been generally held that the placenta grows radially from a fixed centre. Examination of the vascular bed of the placenta has shown, however, that it is bilaterally symmetrical, with the right and left umbilical arteries distributed according to a definite basic pattern consisting of an anterior, lateral, and posterior branch on either side. Right and left sides are recognized by the relation to the umbilical vein, which always lies

anterior to the cross anastomosis between the two arteries. This relation can be demonstrated in the vessels of the 3-mm. embryo at the time when the vascular bed is first established. In the 13-day Torpin ovum the amniotic duct consists of a solid cord of cells in continuity with Langhan's layer of the chorion above, and canalized at its lower end, the lumen opening into the amniotic cavity. It is reminiscent of the strand of cells left along the raphe in those species where the amnion is formed by fusion over the embryonic shield. The amnion is formed by a rearrangement of cells of the embryonic knob around a central cavity. The cells of the knob are in continuity with the chorionic ectoderm at this point, and as these cells are the erosive cells they mark the point of implantation of the ovum in the endometrium. Thus the outer end of the potential amniotic duct underlies the implantation site. In man the allantoic duct makes its appearance at 14 days, and therefore later than the amniotic duct. It extends into the body stalk, and at 21 days reaches as far forwards as the amniotic duct. There is marked undercutting of the body stalk from the chorial plate back to the region of the outer end of the amniotic duct, and this now becomes the outer bed of the potential umbilical cord. This point becomes still further fixed as the vascular bed is established. The authors have been able to identify the cross-anastomosis between the two umbilical arteries in a 3-mm. embryo. This anastomosis fixes the outer end of the body stalk as it becomes the core of the umbilical cord. Hence the placental insertion of the cord marks the normal implantation site.

In most of the grossly bilobate placentas the umbilical cord insertion falls on the line dividing the placenta into two halves. Bilobation is the result of the adaption of the growing villi to the maternal muscular bed, and is not, as has been commonly held, due to extension of growth over the sulci between the anterior and posterior surfaces of the endometrium. From practically any point of implantation, growth of the placenta may be transverse, toward the cervix, or toward the fundus. The most frequent site of implantation is the midline of the fundic zone. Data are given from the Torpin collection consisting of 1,087 specimens. Of these 588 were implanted in the middle of the fundus; 36 were in the right corner and 23 in the left, 5 cervical and 3 cervicolateral.

F. J. Browne

874. **Effect of Pregnancy on the Complement of Guinea Pigs.**
By E. E. ECKER, C. W. HIATT, and L. M. BARR. *J. Lab. clin. Med.* 32, 287–291, Mar. 1947. 4 refs.
The complement titre of serum samples drawn from the marginal vein of the ear of pregnant and non-pregnant guinea-pigs has been compared by determining the amount of serum required to produce 50 per cent haemolysis sensitized sheep cells. A photoelectric colorimeter is used, and to

50 per cent point is estimated by interpolation in von Krogh's equation:

$$x_2 = \text{antilog}\left(\log x_1 - \frac{1}{n} \log \frac{Y}{100 - Y}\right)$$

where x_2 is the amount of serum producing 50 per cent haemolysis, x_1 is the ml. of serum used in the test, and Y is the percentage of haemolysis obtained. The percentage haemolysis should lie between 10 and 90 for von Krogh's equation to apply.

Pregnant guinea-pigs have substantially lower serum concentrations of complement than non-pregnant guinea-pigs; postpartum the complement concentration rises steadily, till at about 5 weeks after parturition it has reached the normal level.

C. L. Oakley

875. **The Rapid Hyperemia Pregnancy Test in Equids. Its Quantitative Evaluation at Different Time Intervals.**
By B. ZONDEK and F. SULMAN. *Endocrinology,* 40, 322–326, May, 1947. 7 refs.

876. **Standardized Radiological Pelvimetry. IV. Interpretation of Pelvimetry.**
By E. P. ALLEN. *Brit. J. Radiol.,* 20, 205–218, May, 1947. 10 figs., 5 refs.
The purpose of this paper is to attempt to establish some basis for prediction by correlating the course of labour with certain features of the pelvis and by trying to determine which features are the most reliable guides to the course of labour. The report on the course of labour was examined, and the case was classed as either normal or abnormal. Labours classed as normal fulfilled the following requirements: (1) The child weighed between 6½ and 8½ lb. (3 to 3.9 kg.). (2) There was no evidence of abnormal moulding of the head. (3) The first stage of labour occupied not more than 20 hours and the second stage not more than 4 hours. (4) An operative procedure when employed was for a condition definitely not related to disproportion.

The abnormal cases were further sub-divided in two ways. In the first place, an attempt was made to assess the level or levels in the pelvis at which disproportion occurred, whether inlet, mid-plane, or outlet. The second sub-division involved "weighting" the abnormal cases by dividing them into the following 3 categories: (1) Cases in which disproportion was minimal; (2) cases in which there was definite disproportion, but in which a normal child could be delivered *per vias naturales*; (3) cases in which delivery *per vias naturales* was impossible. The author admits that this method of dealing with the material may be open to criticism, particularly as he has had to rely for descriptions of labour upon the details provided by the practitioner in charge of each case, and, of course, the standard of obstetrics varied. The correlation between labour and the dimensions

of the pelvis is summarized graphically, the graphs showing variation of the pelvic characteristics against the percentage of weighted abnormal labours.

The author's conclusions are shown in the following table.

Probable mode of delivery	Con-jugate in mm.	Brim area in sq. cm.	Mid-plane area in sq. cm.	Bi-spinous in mm.	Posterior sagittal of outlet in mm.
Vaginal delivery certain; without any evidence of disproportion.	Over 130	Over 130	Over 120	Over 110	Over 65
Vaginal delivery reasonably certain, but there may be evidence of minor disproportion requiring forceps.	105–130	105–130	95–120	90–110	50–65
Vaginal delivery uncertain; will show clear evidence of disproportion.	90–105	85–105	80–95	80–90	45–50
Vaginal delivery extremely unlikely. Elective Caesarean section justified.	Under 90	Under 85	Under 80	Under 80	Under 45

L. G. Blair

877. A Study of Ante-natal Records.
By J. V. WALKER. *Med. Offr.* 78, 91–92, Aug. 30, 1947.

878. Routine Chest Roentgenograms in Pregnancy. A Supplementary Study.
By H. K. GRAHAM. *West J. Surg. Obstet. Gynec.*, 55, 438–441, Aug. 1947. 6 refs.

879. Radiography of the Anencephalic Foetus in Utero. (Radiographies de foetus anencéphale in utero.)
By P. LANTUÉJOUL and R. LEBOUCHARD. *Gynéc. Obstét.*, 46, 327–329, 1947. 4 figs.

880. Placental Radiography with Contrast Substance. (A questão da radiografia placentária sem meio de contraste.)
By O. LACRETA. *Rev. Ginec. Obstet.*, 1, 485–490, June 1947. 5 figs., 7 refs.

881. Nutrition in Pregnancy.
By E. S. EPPRIGHT. *J. Iowa med. Soc.*, 37, 237–239, June 1947. 8 refs.

882. The Diet in Normal Pregnancy. [Sobre alimentacion en el embarazo normal. (Presentación de una cartilla dietética.)]

By O. AVENDANO and J. SANTA MARIA. *Bol. Soc. Chil. Obstet. Ginec.*, 12, 21–27, Apr. 1947.

883. Endocrine Therapy in Obstetrics and Gynecology.
By H. F. TRAUT. *Cincinnati J. Med.*, 28, 453–473, July 1947. 22 refs.

884. The Active Principle of Placental Toxin: Thromboplastin: its Inactivator in Blood; Antithromboplastin.
By C. L. SCHNEIDER. *Amer. J. Physiol.*, 149, 123–129, Apr. 1947. 4 figs., 37 refs.

In an attempt to determine the nature of the toxic substance present in placental extracts which has figured largely but unfruitfully in the literature of eclampsia, the author has compared the thromboplastic and toxic properties of placental extracts [apparently human] in the mouse. He finds closely congruent curves for the decline of these two activities on treatment with serum, heat, and acids, and on dilution. His findings, though not perhaps fully conclusive, are strongly suggestive of identity between the thromboplastic and toxic elements—a fact of considerable importance if placental toxin is to be considered as a possible contributory cause of human eclampsia, since heparin gives protection against it. The author briefly discusses the possible interpretations which such a view would give of the pathology of eclampsia. This work, although somewhat dogmatically presented, will be followed with interest.
Alex. Comfort

882. The Diet in Normal Pregnancy. [Sobre Prediction of Hypertension and Toxaemia in una cartilla dietética.)]
By V. I. KRIEGER and S. WEIDEN. *Med. J. Aust.*, 1, 417–423, Apr. 5, 1947. 5 figs., 12 refs.

Since Hines and Brown described the cold pressor test in 1932 many attempts have been made to pick out early in pregnancy those women who would, later in pregnancy, develop hypertension and pre-eclamptic toxaemia. The results obtained have been variable but on the whole unsuccessful. The authors of the present paper give the results of a new attack on the problem. In a series of 522 cold pressor tests performed during 200 pregnancies all tests gave normal results in 84 patients; there was hyperreaction to the cold stimulus in one test only in each of 31 patients and in more than one test in each of 85 patients; only 13 (15.3 per cent) of the patients, all of whose pressor tests gave normal results, developed hypertension in the later stages of their pregnancies. Of the patients in whom only one of the tests gave a result of the hyperreactive type 50 per cent developed hypertension and pre-eclamptic toxaemia. When there was mild hyperreaction on more than one occasion 26 of the 85 patients had

a normal pregnancy, but 49 developed hypertensive toxaemia and 10 had pre-eclampsia, a total of 69.4 per cent. The authors therefore claim that while the test is not infallible, it serves as a guide to the obstetrician as to whether the patient will develop toxaemia or not.

[It will be noted that the test is based on the hypothesis that in patients who will later develop hypertension there is a *consitutional* vasomotor instability that makes them hyperreactors to the cold pressor test. It has, however, been shown by the abstracter (*J. Obstet. Gynaec. Brit. Emp.*, 1946, 53) that in women who later develop pre-eclamptic toxaemia with hypertension there is no constitutional instability, but that the power to hyperreact is acquired at some time during the pregnancy and, so far as could be observed, after the seventeenth week. May not this account for some of the discrepancies, such as changes in reactivity during the same pregnancy, observed by the authors?]

F. J. Browne

886. **The Eclampsia Problem in the Light of Recent Medical Research.** (Eklampsiproblemet i moderne Belysning.)

By E. MOLLER-CHRISTENSEN. *Ugeskr. Læg.*, 109, 427–434, Aug. 21, 1947. Bibliography.

887. **Pernicious Vomiting in Pregnancy.**

By I. LEWINSKI. *Acta. med. orient.*, 6, 234–236, July 1947.

888. **Eclampsia Puerperarum and Fractura Columnae.**

By P. M. KJELLAND. *Acta. obstet. gynec. scand.*, 27, 297–300, 1947. 1 fig., 4 refs.

890. **Eclampsia with Haemorrhage of the Brain.** (Eklampsie mit Hirnblutung.)

By J. FROEWIS. *Wien klin. Wschr.*, 59, 433–435, July 4, 1947. 1 fig., 3 refs.

891. **Results Obtained by the Treatment of Eclampsia in Pregnancy with Intravenous Sodium Pentothal Injections and Oxygen Inhalations.** (Resultados obtenidos en el tratamiento del sindrome eclamptico en el embarazo, por medio de las inyecciones intravenosas de pentothal sodico e inhalaciones de oxigeno.)

By G. AUBANEL. *Medicina, Méx.*, 27, 250–252, June 10, 1947.

892. **Nephropathies and Pregnancy.** (Néphropathies et grossesse.)

By J. F. PORGE. *Presse méd.*, 55, 325–327, May 17, 1947.

893. **Chorioangioma of the Placenta Associated with Low Implantation and Premature Separation.**

By D. B. ROTH. *Amer. J. Obstet. Gynec.*, 54, 137–139, July 1947. 1 fig., 3 refs.

894. **Placenta Praevia Problem.**

By B. L. KAPUR. *J. Obstet. Gynaec. Lahore*, 8, 54–58, May 1947.

895. **Marginal Placenta Previa Treated by Artificial Rupture of the Membranes Thirty-nine Days before Vaginal Delivery.**

By R. S. MILLEN. *Amer. J. Obstet. Gynec.*, 53, 885, May 1947.

896. **Some Aspects of the Abortion Problem.** (Nägra synpunkter på abortproblemet.)

By P. WETTERDAL. *Nord. Med.*, 34, 1221–1226, May 23, 1947. 11 refs.

897. **Indications for Therapeutic Abortions.**

By Maternal Welfare Committee of the Medical Society for the State of North Carolina. *North Carolina Med. J.*, 8, 367–370, June 1947. 1 fig.

898. **The Treatment of Threatened Spontaneous Abortion.** (Synpunkter på behandlingen av den hotande spontana aborten.)

By P. WETTERDAL. *Nord. Med.* 35, 1575–1577, July 25, 1947. 31 refs.

899. **Oral Therapy in the Management of Threatened Abortion.**

By W. M. SILBERNAGEL. *Ohio St. med. J.*, 43, 739–740, July 1947. 15 refs.

900. **Treatment of Infected Cases of Abortion.** (Die Behandlung der infizierten Fehlgeburt.)

By T. HEYNEMANN. *Dtsch. med. Wschr.*, 72, 273–276, June 6, 1947.

901. **Management of Postabortal Peritonitis.**

By H. C. FALK and G. BLINICK. *Amer. J. Obstet. Gynec.*, 54, 314–320, Aug. 1947. 12 refs.

902. **On What Elements from Curettage Performed for Incomplete Abortion should a Histological Diagnosis be Based?** (Quels sont dans les curetages faits pour " restes d'avortement " les éléments sur lesquels doit se baser le diagnostic histologique de grossesse?)

By R. KELLER. *Gynécologie*, 44, 97–120, May–June 1947. 15 figs.

903. **Spontaneous Rupture of the Uterus.**

By J. T. ELLIS, S. W. WINDHAM, T. K. McFATTER, and S. G. LATIOLAIS. *Sth. Surg.*, 13, 270–279, Apr. 1947. 4 figs., 25 refs.

Two cases of spontaneous rupture of the uterus are recorded, the first in a woman, aged 29, with a history of 3 months' amenorrhoea but no previous pregnancy. She was admitted to hospital on account of intermittent abdominal pains of 8 weeks' duration, associated with vomiting at the onset. Five weeks before admission 1 gallon (4.5 l.) of thin fluid discharged from a rupture in the abdominal wall just below the umbilicus. Two weeks later the discharge became faeculent and

... well advancement ... Three days before admission a foetal arm was extruded from the site of rupture. On examination she was found to be extremely emaciated and dehydrated. The abdomen was covered with apparently faecal material and ... from two sites below the umbilicus, and a macerated foetal arm protruded from a third spot. There was generalised abdominal rigidity and tenderness. Vaginal examination showed a "frozen pelvis". Later tests revealed a positive Kahn reaction and a haemoglobin of 22 per cent. Gas was detected and the bones of a dead foetus were seen on radiograph.

Two and a half litres of whole blood and large quantities of glucose saline were given intravenously, and by this means the haemoglobin level was raised to 70 per cent in 3 days. Thirteen days after admission, incision through a gangrenous abdominal wall revealed a foetus partly extruded from the uterus, which was filled by a darkened foul exudate. The anterior portion of the fundus had sloughed away, as had the lower uterine segment and peritoneum, so that the pelvic brim was exposed. After removal of the foetus, exudate was aspirated and the pelvis drained. In spite of intravenous fluids, the patient died 4 weeks later from sepsis, avitaminosis, and malnutrition. No necropsy was performed.

In the second case, a 37-year-old 4-gravida was admitted to hospital at term complaining of cramp-like abdominal pains, which had been felt frequently during the antenatal period but had been more severe for the previous 12 hours. She was a healthy woman in good condition but with considerable abdominal distension. Foetal parts were readily palpated, but the manner of presentation could not be assessed. The foetal heart-sounds were audible. Pelvic findings were normal, but no presenting part could be identified. Radiography showed a full-time foetus lying transversely below the diaphragm. Ovarian tumour or extra-uterine pregnancy was suspected and pituitrin was given. When no improvement in contractions resulted, Caesarean section was advised. There were 5 litres of greenish fluid and a large foetus free in the peritoneal cavity. The placenta was attached to the ruptured fundus of the uterus, and peritonitis was present. Uterus and appendages were removed. The patient died shortly after operation, but the infant survived.

The authors discuss the aetiology of ruptured uterus and review some of the literature. The incidence found at various obstetric centres varies from 1 in 95 to 1 in 4,000 deliveries. Classical Caesarean section, myomectomy, too energetic curettage, and pelvic infection are regarded as important predisposing causes. Rupture in pregnancy is more often fundal, whereas in labour the lower segment is more commonly involved. It occurs more often in multiparae than in primigravidae. Caution is needed in differentiating between uterine inertia and ruptured uterus with cessation of labour. In oxytocics be prescribed in the latter condition. Laparotomy, preceded if necessary by blood transfusion, is the treatment of choice, and if infection be present surgery should be radical. Maternal mortality range from 50 to 100 per cent, and foetal mortality is said to be 90 per cent.

Doreen Daley

905. **Concealed Rupture of the Uterus.**
By M. E. GARDNER. *Ohio St. med. J.*, 43, 841-842, Aug. 1947. 3 refs.

905. **Uterine Rupture.**
By I. DONALD. *Proc. R. Soc. Med.*, 40, 379-380, May 1947.

906. **Rupture of the Uterus.**
By J. S. TAYLOR. *Penn. med. J.*, 50, 801-807, May 1947. 2 refs.

907. **Rupture of the Uterus. A Case Report with Review of Literature.**
By C. A. JAMES. and C. H. LIGON. *Delaware St. med. J.*, 19, 120-121, June 1947. 14 refs.

908. **Rupture of the Uterus Following Cesarean Section.**
By M. S. MUSA. *J. Palestine Arab med. Ass.*, 2, 95-99, May 1947. 3 refs.

909. **The Management of Ovarian Tumors Complicating Pregnancy.**
By H. C. FALK. and I. A. BUNKIN. *Amer. J. Obstet. Gynec.*, 54, 82-87, July 1947. 16 refs.

910. **Notes on a Case of Cancer of the Cervix Uteri and Pregnancy.** (Sobre un caso de cancer de cuello uterino y gestación.)
By B. BLANCO. *Toko-ginec. práct.*, 6, 161-173, May 1947.

911. **Degenerating Tumors Complicating Pregnancy. Myomectomy in the Prenatal Period.**
By E. F. ANDERSON. *West. J. Surg.*, 55, 273-277, May 1947. 18 refs.

912. **The Significance of Decidual Polyps in Otherwise Normal Pregnancies.**
By R. L. HASS. *Amer. J. Obstet. Gynec.*, 54, 124-126, July 1947. 4 refs.

913. **Hemoperitoneum from Rupture of the Corpus Luteum. Report of a Case of Ruptured Corpus Luteum of Pregnancy.**
By J. PEEMAN. *Pennsylvania med. J.*, 50, 1161-1163, 1947. 6 refs.

914. **Torsion of the Full Term Pregnant Uterus.**
By F. R. STANSFIELD. *Clin. J.*, 76, 183-184, Sept.-Oct. 1947. 3 refs.

915. **Pregnancy and the Double Uterus.**
By T. D. TYSON. *Amer. J. Obstet. Gynec.*, 53, 869-872, May 1947. 3 refs.

916. A Case of Uterus Duplex with Simultaneous Pregnancy in Both Uterine Cavities. (Fall av uterus duplex med samtidig graviditet i båda uterinhålorna.)

By L. G. HALLÉN. *Nord. Med.*, 34, 1069–1070, May 2, 1947.

917. Peptic Ulcer with Hemorrhage during Pregnancy and Fetal Death.

By E. B. LE WINN. *Amer. J. Obstet. Gynec.*, 54, 114–118, July 1947. 8 refs.

918. The Obstetric Managment of Pregnancy Complicated by Heart Disease.

By D. N. HENDERSON. *Amer. J. Obstet. Gynec.*, 53, 494–499, Mar. 1947. 2 refs.

This paper reports an analysis of 200 consecutive cases of pregnancy complicated by heart disease occurring at Toronto General Hospital since 1938. Thirty patients were treated by the induction of abortion; of these 20 had had 2 or more living children and only 2 were primiparae. Indications for induction of abortion were cardiac failure during pregnancy, previous marked impairment of exercise tolerance, or severe myocarditis. These patients were sterilized at the time of operation where practicable. One patient died from cardiac failure 30 days after termination of pregnancy. Among the 170 remaining patients 40 went into premature labour, 4 after induction. Of the patients who went to term, 22 were delivered by Caesarean section, but this method has been largely given up in the last 13 years. The general management of cardiac patients consisted of rest during pregnancy and administration of sedatives during labour, with forceps delivery if the second stage of labour was likely to be prolonged. There were 8 deaths in the 200 cases. Four of the deaths occurred in patients admitted in emergency; there were 21 emergencies in all, so that the corrected mortality for booked cases was 2.2 per cent. The average age at death was 38.8 years, which is one year higher than the average age of 56 female patients shown at necropsy to have died from rheumatic heart disease not associated with pregnancy.   *D. M. Stern*

919. The Cardiac in Pregnancy.

By F. R. HOOD. *Oklahoma J. med. Ass.*, 40, 181–184, May 1947.

920. Report from Cardiac Clinic of the Boston Lying-in Hospital for the First Twenty-five Years.

By B. E. HAMILTON. *Amer. Heart J.*, 33, 663–668, May 1947.

921. Pregnancy Complicated by Coarctation of the Aorta.

By E. R. NOVAK. *Amer. J. Obstet. Gynec.*, 53, 1054–1056, June 1947. 6 refs.

922. Subacute Bacterial Endocarditis During Pregnancy.

By M. E. DAVIS and R. F. WORTMANN. *Amer. J. Obstet Gynec.*, 53, 878–880, May 1947. 1 fig.

923. Hypoprothrombinaemia and Cerebral Injury in a Newborn Infant after Dicoumarol Treatment of the Mother. (Hypoprotrombinemi och hjärnskada hos barn till dikumarinbehandlad mader.)

By G. V. SYDOW. *Nord. Med.*, 34, 1171–1172, May 16, 1947 1 fig., 3 refs.

A woman aged 44 was given dicoumarol for 1 month before delivery on account of a thrombus in the left leg. Her prothrombin index fell during treatment until it reached 33 on the day of delivery and 16 two days later. It was quickly restored to normal by administration of vitamin K, and there was no excessive haemorrhage during delivery. Examination of the child some hours after birth revealed that there had been extensive subcutaneous haemorrhages over the forehead and scalp; small petechiae were also found in the palate and pharynx. The prothrombin index was found to be extremely low (below 10) and the Hb value comparatively so (94 per cent). Despite intensive treatment with vitamin K, the prothrombin index remained low for 6 days, after which it suddenly returned to normal. The general condition of the child was satisfactory, but it was noticed that when the mother and child were discharged 3 weeks after the birth the child's skull was strikingly large. Subsequent examination showed that the maximum diameter of the skull had increased by the seventh week from 36 cm. at birth to 41.5 cm. Neurological examination showed that there was free communication between the ventricles and the subarachnoid space. At 5 months the maximum diameter was 53 cm. The author points out that hyperprothrombinaemic mothers give birth to children whose prothrombin indices are above the normal, and suggests that when the converse occurs the condition of the child is also a direct consequence of the condition of the mother. In the present case the low prothrombin indices of both mother and child were due to the dicoumarol treatment, and the hydrocephalus was presumably the result of intracranial haemorrhage corresponding to the subcutaneous haemorrhage observed on the scalp. The writer warns against the administration of dicoumarol to pregnant women.
                                    B. Nordin

924. Anaemic Syndrome with Erythraemic Characters Arising in Pregnancy. (Sindrome anemica ad impronta eritremica insorta in gravidanza.)

By U. BRACALE. *Arch. Ostet. Ginec.*, 52, 234–247, July–Aug. 1947. 4 figs., 7 refs.

925. Purpura Thrombopenica in Pregnacy. (Purpura thrombopenica—graviditas.)

By P. GUNDERSEN. *Nord. Med.*, 35, 1829–1831, Sept. 5, 1947. 9 refs.

926. Brain Tumour in Pregnancy. (Tumor cerebral e gravidez.)

By D. G. COSTA. *An. brasil. Ginec.*, 12, 108–118, Feb. 1947. 9 figs., 5 refs.

927. Adenoma of the Islets of Langerhans in Pregnancy. (Adenoom van de eilandjes van Langerhans en zwangerschap.)

By A. W. M. POMPEN, C. A. L. JANSEN, and J. DHONT. *Ned. Tijdschr. Geneesk.*, 90, 1791–1795, Nov. 30, 1946. 2 figs., 16 refs.

A peasant woman, aged 34, 13 days after her second confinement, had sudden attacks of unconsciousness with sweats and increased salivation. Within minutes she began to improve spontaneously, but when consciousness returned she could not speak for a while, her arms felt tired, and she had diplopia, hazy vision, and a queer sensation in the occiput. Between attacks she was normal. Her past history also was normal. The attacks, recognized as hypoglycaemic, ceased after administration of 20 per cent glucose intravenously. During the attacks the blood sugar was 0.05 to 0.06 per cent; her blood pressure was 150/110 mm.; and her ankle jerks were increased. The sella turcica was normal. Urine and erythrocyte sedimentation rate were both normal. The blood calcium content was 11 mg. per 100 ml. After the administration of 50 g. of glucose by mouth the blood sugar was 0.221 per cent after 1½ hours, and 0.143 per cent after 2½ hours. After ceasing breast feeding, 71 days after delivery, there were no more severe attacks. A month later attacks started again, and the patient took large quantities of sugar as a preventative. When she again became pregnant she felt much better. She gave birth to another healthy baby about 17 months after the second. Nine days later the attacks started once more, recurring daily. She lost consciousness for 6 to 12 hours or had severe headaches and dizziness with vomiting, screaming fits, and complete confusion, while her speech became indistinct. Later a left hemiparesis occurred. All these symptoms could be prevented only by giving her 100 to 150 g. of sugar a day. Her blood sugar was now 0.02 to 0.07 per cent. She was operated upon 60 days after her confinement, as an adenoma of the pancreas was suspected. In the head of the pancreas a tumour the size of a hazel nut was removed; there was an immediate rise in the blood sugar. On microscopical examination the tumour proved to be an adenoma of the islets. Several complications prolonged recovery, which took 67 days. The fasting blood sugar now became 0.103 to 0.128 per cent.

The interesting fact in the case is that she had two normal pregnancies during which she felt well, while shortly after the confinements deterioration set in. As the 24-hour blood-sugar curves show, there were, after the first pregnancy, great fluctuations between hyper- and hypoglycaemia, whereas after the second pregnancy the entire curve remained very low. In similar cases of islet adenoma the symptoms have also disappeared with pregnancy, only to return after confinement.

Investigations by Young supply a possible explanation. He found that a " glycotrophic factor " or " anti-insulin " is present in the anterior pituitary which, without influencing the blood-sugar curve, decreases or suppresses the effect of insulin on the blood sugar and on glycogen fixation in the muscles. If the greater activity of the pituitary during pregnancy also extends to a greater production of this substance the phenomenon is explainable. *B. Baneth*

928. Effect of Thiouracil Compounds on the Baby. (Om Virkningen af Tiouracilforbindelser paa Fosteret.)

By E. FREIESLEBEN and K. KJERULF-JENSEN, *Nord. Med.* 32, 2811–2812, Dec. 6, 1946. 8 refs.

The authors refer to the literature on the effect on the mother and child of thiouracil given in pregnancy, and add details of a case of their own in which pregnancy had to be terminated in the fifth month. The foetal thyroid was found to be much larger than normal and hyperplastic. The greater part of the paper, however, is devoted to their experiments on rats. Pregnant rats were fed on a standard diet with relatively large amounts of propylthiouracil for some days, after which the foetuses were removed, dried, pulverized, and then fed to normal rats. The thyroids of these animals showed typical hyperplasia; this is taken as proof that thiouracil can pass across the placental membrane. Next, methylthiouracil was given to pregnant rats in doses comparable with those used in man (0.25 mg. in 10 g. of food) and this dosage was continued from conception to delivery. The mothers developed goitres, but the newborn rats showed only a transient thyroid hyperplasia. When the thiouracil dosage was continued during lactation, however, the newborn rats showed marked hyperplasia, which disappeared in a month after stopping the mother's thiouracil, but their further development was slightly retarded permanently. If the growing rats were given the drug in their own food as well (when weaned) they developed a typical cretinism. This could be prevented by giving thyroid hormone, the drug was thus acting through the thyroid and not directly. These results confirm and extend the observations of Hughes (*Endocrinology*, 1944, 34, 39).

As regards the human mother and child, the authors consider, in view of the fact that the thyroid hormone and the thyrotrophic hormone can probably both traverse the placental membrane, the child of a woman given thiouracil provided that the dose is not too large. The drug is [...] mother is [...]

This well-known American authority on diabetes in pregnancy reviews the results of pregnancy in 300 consecutive cases seen between 1936 and 1946 in which the gestation lasted at least 24 weeks. There were 51 foetal deaths; 1 maternal death occurred from infective hepatitis. The abnormalities found when pregnancy complicates diabetes are classified as: (1) *Maternal*: (a) vascular disease, present in 70 per cent of patients who have survived 20 years of diabetes, and (b) hypo-ovarianism. (2) *Obstetric*. These include irritable uterus (in 1 per cent the membranes ruptured long before labour began), early spontaneous abortion (25 per cent), pre-eclampsia (40 per cent; where it was abnormal (58), only 47 per cent. There are low renal threshold for glucose, disturbance of water balance (oedema, hydramnios), and imbalance of sex hormones. (4) *Foetal*. Physically, large size of the foetus is common, as are defects, jaundice, and atelectasis. Chemically, an unstable blood sugar is found. Pathologically, a syndrome resembling erythroblastosis without anaemia in an Rh-positive mother occurs. (5) *Placental Defects*. These include too large and too small an organ.

The most important of these factors is the sex-hormone imbalance. Where this balance was normal (66 cases), 99 per cent of the foetuses survived and the incidence of pre-eclampsia was 2 per cent; where it was abnormal (58), only 47 per cent of the foetuses survived and the pre-eclampsia incidence was 50 per cent. Hence the need for supplying the missing hormones, oestrogen and progesterone. When this was done in 174 cases the foetal survival rate rose to 90 per cent and the incidence of pre-eclampsia fell to 5 per cent.

The rules for management of the diabetic obstetric patient include induction of premature labour at the end of the thirty-seventh or beginning of the thirty-eighth week (Caesarean section was performed on two-thirds of this series), minimal medication, and the use during labour (or pre-operatively and postoperatively) of 1,000 ml. of 5 per cent glucose solution. Salt and sodium bicarbonate are restricted during pregnancy, and ammonium chloride (1 to 2 drachms: 4 to 8 g.) is given daily if oedema occurs.

Stilboestrol and " proluton " (progesterone) are administered during pregnancy by daily intramuscular injection of 5 mg. of each up to the twentieth week; 10 mg. from the twentieth to the twenty-fourth; 15 mg. from the twenty-fourth to the twenty-eighth; 20 mg. from the twenty-eighth to the thirty-second; 25 mg. from the thirty-second to the thirty-sixth; and 30 mg. from the thirty-sixth until delivery. Thyroid and vitamin E are also given.

S. S. B. Gilder

930. Diabetes and Pregnancy. (Diabetes en zwangerschap.)
By B. S. Ten Berge and J. J. Van Assen. *Ned.*

Tijdschr. Geneesk., **91**, 1229–1233, May 17, 1947. 7 refs.

931. Diabetes Insipidus in Pregnancy: Report of a Case with Disordered Action of Uterine Muscle.
By M. Lake. *Med. J. Aust.*, **2**, 206–209, Aug. 16, 1947. 3 figs., 10 refs.

932. Effects of Diabetes Mellitus on Foetus.
By H. Bahry. *J. Obstet. Gynaec. Lahore*, **8**, 51–53, May 1947.

933. Rapid Treatment of Prenatal Syphilis.
By S. Olansky and R. Beck. *Amer. J. Syph.*, **31**, 51–56, Jan. 1947. 2 refs.
Although congenital syphilis can be prevented, thousands of infected infants are born in the United States each year. The authors conclude that many syphilitic women do not receive adequate treatment during pregnancy, and believe this failure to be due to the fact that standard methods of antisyphilitic treatment take too long and are too difficult for the average patient. [In Britain congenital syphilis usually follows failure to diagnose maternal syphilis; the known syphilitic mother is usually co-operative, and attends well for treatment throughout her pregnancy.] The authors have therefore studied intensive-treatment methods in an attempt to prevent prenatal syphilis, and here report the results in 147 patients, of whom 129 were studied for 3 months or longer after confinement. In this series there were 128 live births, 5 abortions, and 6 stillbirths. The 128 live infants were free from clinical signs of syphilis, and only 1 had persistently positive serological evidence. In 2 cases of stillbirth, the foetus showed no pathological evidence of syphilis, and in another 2 cases it was considered that the foetus, which was macerated at birth, had died before treatment was started. One of the abortions was considered to be traumatic in origin, and in another the foetus was thought to be dead before treatment was started.

The treatment schedules used were: (1) 1,200 mg. " mapharsen " by slow intravenous drip over 5 or 8 days combined with 0.2 g. bismuth subsalicylate weekly for 8 weeks; (2) 60 injections of 40,000 units of penicillin at 3-hourly intervals; (3) (a) 1 mg. mapharsen per kilo body weight (maximum of 60 mg. per dose) daily for 8 injections, 10,000 units of penicillin every 3 hours for 60 injections, and 0.2 g. bismuth subsalicylate on the first, fifth and ninth days; (3) (b) injections of mapharsen on the first, third, fifth, seventh and ninth days, 16,667 units of penicillin intramuscularly every 3 hours for 72 injections, and 3 injections of 0.2 g. bismuth subsalicylate. The stage of syphilis and point in pregnancy at which treatment was started and the outcome of the pregnancies are reported in detail. The findings justify the authors' conclusion that intensive antisyphilitic treatment even late in pregnancy results in a high proportion of non-syphilitic infants.

S. M. Laird

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S. M. Laird

934. Syphilis in Pregnancy Treated by Penicillin.

By C. H. INGRAM. *Amer. J. Obstet. Gynec.*, 53, 881–882, May 1947. 4 refs.

935. Serodiagnostic Syphilis Control of Pregnant Women. (Serodiagnostisk syfiliskontroll av gravide kvinner.)

By T. M. VOGELSANG. *Tidsskr. norske lægeforen.*, 67, 226–228, May 1, 1947.

936. Acute Poliomyelitis in Pregnancy. Report of Thirty Cases.

By M. E. BAKER. and I. G. BAKER. *Minnesota Med.*, 30, 729–734 and 758, July 1947. 17 refs.

937. Premature Delivery and Stillbirth in Malarial Patients.

By M. L. RENIGER-ARESHEVA. *Akush. Gynek.*, 1, 20–25, 1947. 2 figs. [In Russian.]

Of 248 expectant mothers suffering from malaria 100 (40.3 per cent) had a miscarriage and 37 (15 per cent) had a premature labour; thus 55.3 per cent of pregnancies in malarial mothers did not reach term. The usual time at which the pregnancy terminated spontaneously was between the fifth and seventh months. Two lines of research have been particularly followed : (1) an investigation into the histology of the placenta in malarial patients; (2) estimation of the vitamin-C content of the various organs of the foetus. The placental villi showed accumulations of malarial pigment in the portions of the stroma from which the syncytium was absent; there were also proliferation of the syncytium with deposition of malarial pigment, hyaline degeneration of the villi, calcification of the vessels, and numerous cells full of malarial pigment lying free in the intervillous space. Vitamin C was either absent or very deficient in the foetal part of the placenta and in all the foetal organs in the cases examined. Altogether 29,636 deliveries took place in the area in 25 years (1920–1944); of these 2,213 (7.5 per cent) resulted in premature deliveries; 996 (45 per cent) of these patients suffered from malaria. In a series of 40 full-time deliveries of mothers with active malaria there were 3 stillbirths (7.5 per cent), of the remaining 37 infants only 15 (37.5 per cent) survived the neonatal period. The author concludes that a malarial mother has less chance of producing a viable full-time foetus than a non-viable one. It is emphasized that malaria must be treated especially energetically during pregnancy.

Nicolas Tereshchenko

938. Tuberculosis and Pregnancy. A Clinical and Statistical Study of 123 Cases. (Tuberculose et grossesse. Étude clinique et statistique de 123 cas.)

By J. A. MITTI and J. L. PILLON. *Un. méd. Can.*, 76, 815–818, July 1947. 10 refs.

939. Renal Tuberculosis and Pregnancy. (Tuberculose rénale et grossesse.)

By — BORROU. *J. Méd. Bordeaux*, 124, 350–356, Aug. 1947.

940. Some Remarks on Pyelitis and Pyelonephritis in Pregnancy and their Treatment. (Quelques remarques à propos des pyélites et pyélonéphrites gravidiques et de leur traitement.)

By E. LARTIGAUD. *Rev. franc. Gynéc.*, 42, 218–224, June 1947. 8 refs.

941. Possiblity of Extrauterine Pregnancy in Ovarian Endometriosis. (Possibilità di gravidanza extrauterina nelle endometriosi ovariche.)

By A. NORDIO. *Arch. Ostet. Ginec.*, 51, 357–365, Nov.–Dec. 1946. 6 figs., 19 refs.

The possibility of implantation of a fertilized ovum on an ovary the site of endometriosis has been discussed by several authors. Primary ovarian pregnancy is a relatively rare occurrence and is usually due to intrafollicular nidation of the fertilized ovum. In such a case the corpus luteum is found in the same ovary as the pregnancy.

The author describes the case of a woman of 25 in whom menstruation was previously regular. When the last period was 5 to 6 days overdue she experienced haemorrhage and pain. A diagnosis of metropathia haemorrhagica was made. At laparotomy the uterus was found to be enlarged and the right ovary to contain a typical corpus luteum of pregnancy. The left Fallopian tube was normal, but the left ovary contained a small blood cyst. The left ovary and the uterine fundus were removed. The uterine muscle showed no sign of adenomyosis. The left ovary showed a diffuse decidual reaction. Numerous chorionic villi were found in the ovary and also typical endometrial glands with decidual reaction.

The author points out that the possibility of implantation of a fertilized ovum in an ovary the site of endometriosis has rarely been confirmed. The presence of the corpus luteum in the opposite ovary confirms this possibility. This case record represents a new contribution to the study of migration of the fertilized ovum. The diffuse decidual reaction in the ovary is of particular diagnostic value. Difficulty arose in the author's case because no trace of the embryo could be found, because interruption of the pregnancy occurred before the patient had noticed any abnormality, because of the absence of amenorrhoea, and because of the incongruous association of a small cyst with well-developed chorionic villi.

[This is a very interesting case record. The association of pregnancy and endometriosis is an uncommon one. It is generally held that the sterility in these cases is due to the disturbance of ovarian function associated with extensive deposition of endometrial tissue. The occurrence of ovarian pregnancy in deposits of endometriosis is certainly a possibility and it is perhaps remarkable that it does not occur more often, especially in cases where the lesion is early and superficially situated.

Joseph Barnes

942. **Ectopic Pregnancy. An Analysis of 67 Consecutive Cases.**

By M. J. THORNTON. *Wisconsin Med.*, **46**, 691–693, July 1947. 6 refs.

943. **Decidua Formation in Ectopic Pregnancy.** (Decidua vorming bij ectopische zwangerschap.)

By P. BRUSSELMANS. *Belge. Tijdschr. Geneesk.*, **3**, 487–490, June 1947. 9 refs.

944. **Simultaneous Intrauterine and Extrauterine Pregnancy.**

By C. POWELL and R. H. GOTTSCHALK. *Amer. J. Obstet. Gynec.*, **54**, 132–134, July 1947. 5 refs.

945. **Statistical Observations on Extrauterine Pregnancy in Saturnino Lora Hospital, 1943-46.** (Observaciones estadisticas sobre el embarazo extrauterino en el Hospital S. Lora durante los años 1943-46.)

By R. G. ESTRADA LERROUX. *Rev. méd.-quirúrg. Oriente*, **8**, 75–79, June 1947.

946. **Full-Term Intraligamentary Pregnancy.**

By I. T. FRASER. *Proc. R. Soc. Med.*, **40**, 378–379, May 1947. 2 refs.

947. **Tubal and Uterine Twin Pregnancy.**

By M. O. BELSON. *Amer. J. Obstet. Gynec.*, **53**, 883–884, May 1947.

948. **Early Tubal Pregnancy.**

By R. K. DEWAR. *Canad. med. Ass. J.*, **57**, 288–289, Sept. 1947.

949. **Recurrent Tubal Pregnancy.**

By A. F. LEE. *Northw. Med., Seattle*, **46**, 535–536, July 1947. 7 refs.

950. **A Rare Ectopic Pregnancy in the Left Cornu of the Uterus.** [In English.]

By A. WIST. *Ann chir. gynaec. fenn.*, **36**, 129–141, 1947. 9 figs., 44 refs.

951. **Primary Ovarian Pregnancy.**

By N. P. ISBELL and W. B. BACON. *Amer. J. Obstet. Gynec.*, **45**, 329–335, Aug. 1947. 4 figs., 31 refs.

952. **Abdominal Pregnancy.**

By L. H. DOUNGLASS and S. G. KOHN. *West Virginia med. J.*, **43**, 307–310, Sept. 1947. 4 figs.

LABOUR

953. **Delayed Ligation of the Umbilical Cord.**

By G. N. BALLENTINE. *Pennsylvania med. J.*, **50**, 726–728, Apr. 1947. 5 refs.

Immediate ligation of the cord on delivery of the infant has been shown to lead to a lowering of the erythrocyte count and haemoglobin value in the first week of life as well as to an iron deficiency later. The practice may also contribute to the hypoprothrombinaemia of the newborn.

In a series of 135 deliveries (vertex presentations) studies were made of the amount of blood obtained by the infant as a result of delaying ligation of the cord. All but one patient were delivered spontaneously or by low forceps, and all received an intravenous injection of " ergotrate " when the anterior shoulder was delivered, so that delivery of the placenta was prompt. Thirty infants were delivered directly on to scales; the cord was at once ligated and cut, and the infant weighed. It was again weighed 30 to 40 minutes later. The change in weight was negligible. A second group of 30 infants were delivered on to scales and weighed. The cord was not ligated, and the baby and placenta were transferred to a cradle. After the cord had stopped pulsating it was ligated and cut, and the infant was again weighed. The average gain in blood volume (calculated from the specific gravity of blood and the gain in weight) was 96 ml., with extremes of 37 and 187 ml. There was no relation between the weight of the baby, the length of the cord, and the length of time elapsing before the cord ceased to pulsate (average 21.7 minutes). Elevation of the placenta during the immediate postnatal period did not result in increased gain in weight. In a group of 5 infants 55 per cent of the blood gained after birth flowed into the infant in the first minute and 84 per cent in the first 5 minutes.

In a group of 20 infants the cord was found to contain an average of 0.63 ml. of blood per centimetre. When the cord was immediately clamped at the placental end in another group and then ligated at the umbilicus after it had stopped pulsating, it was found to contain only 0.072 ml. of blood per cm., so that immediate clamping of the cord at the placental end with later ligation at the usual site will result in a gain of 20 to 30 ml. of blood to the average infant.

S. S. B. Gilder

954. **Full-Term Labor after a Subtotal Hysterectomy in Double Uterus.**

By H. ACOSTA-SISON. *Amer. J. Obstet. Gynec.*, **54**, 129–131, July 1947. 3 refs.

955. **The Management of Delivery Following Stillbirth from Previous Dystocia.**

By A. B. HUNT. and R. W. DE VOE. *Amer. J. Obstet. Gynec*, **53**, 812–816, May 1947. 1 ref.

956. **Active Conduct of Labour in Breech Presentations.** (Zur aktiven Geburtsleitung bei Beckenendlagen.)

By F. HOFF. *Wien. klin. Wschr.*, **59**, 381–385, June 13, 1947. 3 figs., 10 refs.

957. **The Management of Breech Presentation.**

By D. F. ANDERSON. *Med. Press*, **217**, 434–436, May 21, 1947.

958. **Management of Breech Presentation.**

By J. M. WHITFIELD. *West Virginia med. J.*, **43**, 266–269, Aug. 1947.

959. The Genesis of Central Rupture of the Cervix Uteri. (Zur Genese der zentralen Cervixruptur.)

By A. Stingel. *Wien. klin. Wschr.*, 59, 462–464, July 18, 1947. 17 refs.

960. Acute Postpartum inversion of the Uterus. (Inversão aguda do útero posparto.)

By J. Dias Ayres. *An. paul. Med. Cir.*, 53, 309–316, May 1947. 1 fig., 12 refs.

961. Postpartum Hemorrhage and Shock.

By R. D. Mussey. *J. med. Ass. Georgia*, 36, 251–258, July 1947. 7 refs.

962. Prophylactic Use of Penicillin in Retained Placenta. (Beitrag zur prophylaktischen Anwendung des Penicillins bei Plazentarresten.)

By E. Navratil. *Wien. klin. Wschr.*, 59, 363–365, June 6, 1947. 14 refs.

963. Monoamniotic Twins.

By D. Coulton, A. T. Hertig and W. N. Long. *Amer. J. Obstet. Gynec.*, 54, 119–123, July 1947. 8 refs.

964. A Further Description of a Set of Quadri-ovular Quadruplets. (A Study of Dermal Configurations and Tooth Eruption.)

By N. F. Walker. *Amer. J. Obstet. Gynec.*, 54, 266–272, Aug. 1947. 2 figs., 17 refs.

ANAESTHETICS, ANALGESICS

965. Anesthesia in Obstetrics.

By J. P. Greenhill. *Amer. J. Obstet. Gynec.*, 54, 72–81, July 1947. 22 refs.

966. Painless Childbirth.

By O. Schmahmann. *S. Afr. med. J.*, 21, 597–600, Aug. 23, 1947. 27 refs.

967. Combined Evipal and Scopolamine Analgesia and Cyclopropane Anesthesia in Obstetrics.

By H. E. Anderson. *Amer. J. Obstet. Gynec.*, 53, 758–765, May 1947. 12 refs.

In a series of 700 obstetric cases analgesia was effected by the use of " evipan sodium " (hexobarbitone soluble) rectally, together with scopolamine hydrobromide hypodermically, and cyclopropane anaesthesia at the time of delivery. Reference is made to a previous series of 53 cases in which the same analgesics were used, but second-stage anaesthesia was produced by open ether, and also to reports by other workers of success with these preparations.

The drugs were administered when: (1) the patient was definitely in labour; (2) complaint was made of pain; and (3) the cervix was taken up and 2 to 3 cm. dilated. Evipan, 1.5 g., was dissolved in 60 ml. of tap water and allowed to run into the rectum through a funnel by gravity, a soft rubber catheter being inserted high enough to introduce the solution above the presenting part. Scopolamine hydrobromide, gr. 1/150 (0.4 mg.) was given hypodermically at the same time and

repeated in doses of gr. 1/200 (0.32 mg.) after an hour or later in labour as required for good amnesia; the second dose was required in only 25 per cent of cases. Cyclopropane anaesthesia was used only when delivery was imminent and the patient had been transferred to the delivery room.

A satisfactory degree of analgesia and amnesia was obtained. Undue excitement during a pain occurred in 5 per cent of patients, but all had complete amnesia. Constant nursing attendance was necessary; 1½ to 2 hours' sleep after delivery was usual. Early in the series a number of patients who had had castor oil for induction of labour failed to obtain complete amnesia, but with abandonment of the use of castor oil no further failures occurred. No maternal deaths were recorded, and the duration of labour was not increased; too early administration of the drugs may cause labour to cease. There is no evidence that the method is unsuitable for toxaemic patients. The normal technique of administration of cyclopropane was employed, but elaborate precautions were taken against the risk of explosion.

The 705 babies delivered included 5 sets of twins; there were 674 vertex and 31 breech presentations. There were 4 stillbirths—1 due to meningocele, 1 to prematurity with placenta praevia, 1 to intrauterine death at 17 weeks, and 1 to prolapsed cord. Foetal asphyxia did not occur and only 50 babies required resuscitation; no evidence was found of ill effects through analgesia late in labour. Lacerations which required suture were encountered 31 times, and in 1 case the cervix was deliberately incised to facilitate delivery.

Low-forceps delivery was performed in 312 cases, and mid-pelvic forceps application was needed in 47. The author has no hesitation in applying low forceps to shorten labour and reduce trauma to the foetal skull; there was no increase in the incidence of mid-pelvic forceps deliveries.

The patients were mainly of Northern European stock and had been adequately prepared psychologically for labour. Nitrous oxide and ether are mentioned as having an inhibitory effect on the uterus and on the foetal respiratory centre. Local pudendal block with 1 per cent " novocain " (procaine) was found satisfactory, in the absence of an anaesthetist. The high oxygen ratio used with cyclopropane is said to be partly responsible for the low rate of infant resuscitation. An increase in the low-forceps rate is admitted, but is stated to be no greater than with any other barbiturate; there was an absence of local rectal reaction. It is suggested that the cervical laceration rate of 4 per cent is a tribute to the relaxing qualities of the drugs used.

Hugh R. Arthur

968. Sigmodal in Obstetrics. Clinical Observations with a Report of Three Reactions.

By A. M. Lilienfeld and D. McC. Dixon. *Bull. Sch. Med., Maryland*, 31, 135–143, Apr. 1947. 7 refs.

The effect of " sigmodal " (5-sed. amyl-5-beta-bromallyl barbituric acid) in labour was studied in a total of 391 patients. This little known barbiturate was clinically investigated first by Emmert and Goldschmidt in 1936; these authors published their results in a final series of 550 cases in 1941. A series of 166 cases was reported by Watson in 1942. In the present cases the drug was administered through a thin urethral catheter into the rectum. A dose of 3 gr. (0.2 g.) of " seconal " was given when the patient became uncomfortable, and the sigmodal was given when the cervix was 4 cm. dilated in a primigravida or, regardless of cervical dilatation, when uterine contractions were lasting for at least 35 seconds in a multipara. Within 5 to 15 minutes of the patient's receiving and retaining the sigmodal she shows signs of increasing drowsiness and generally falls asleep. A second dose is sometimes necessary. The first dose consists of 10 ml. of the preparation; the second, when needed, of not more than 5 ml. This dose may be repeated every 3 or 4 hours. In about 90 per cent of cases delivery is accomplished by episiotomy and the use of low forceps. A total of 223 cases was analysed for amnesic effect. In 75.3 per cent there was complete amnesia; in 16.2 per cent almost complete or partial amnesia; and in 8.5 per cent no amnesic effect was obtained. The drug appeared to have no effect upon blood pressure, pulse rate, respiration rate, or foetal heart rate, and 83.6 per cent of infants did not require any active resuscitation. Excitement and muscular twitchings were seen in a varying number of patients. In 3 cases severe respiratory depression occurred. These serious reactions may have been caused by variations in the nature of the drug, but were more probably due to overdosage and to the added anoxaemic effect of nitrous oxide. The question of over dosage is being further studied by means of blood-level determinations.

Falkland L. Cary

969. **Self-induced Nitrous Oxide Analgesia in Labour.** (Autoanalgésie obstetricale au protoxyde d'azote.)

By P. LANTUÉJOUL, J. BOUREAU and R. CHAMBRAUD. *Gynéc. Obstét.*, 46, 293–297, 1947. 2 figs., 6 refs.

970. **Oxygen Therapy and Obstetric Analgesia by Nitrous oxide in Closed Circuit.** (Oxygénothérapie et analgésie obstétricale au protoxyde d'azote en circuit fermé.)

By J. SCÉMLA. *Bull. méd., Paris*, 61, 311–312, July 21, 1947.

971. **Saddle Block Anesthesia in Obstetrics. A Preliminary Survey of 50 Cases.**

By E. L. KING and I. DYER. *New Orleans med. surg. J.*, 100, 70–72, Aug. 1947.

972. **Use of Caudal Anesthesia in Obstetrics.**

By D. WALL. *J. Iowa St. med. Soc.*, 37, 201–202, May 1947. 1 ref.

973. **Can Spinal Analgesia Nowadays be used Without Danger in Obstetrics?** (Peut-on utiliser de nos jours sans danger l'anesthésie rachidienne en obstétrique?)

By P. PAQUET. *Rev. franc. Gynéc. Obstét.*, 42, 198–202, June 1947. 5 refs.

974. **Spinal Anesthesia for Pelvic Delivery.**

By P. S. MARCUS, J. W. TUNNELL and L. H. WILKINSON. *New Engl. J. Med.*, 237, 258–261, Aug. 21, 1947. 11 refs.

975. **Painless Labors Following Presacral Neurectomy.**

By G. BLINICK. *Amer. J. Obstet. Gynec.*, 54, 148–151, July 1947. 20 refs.

PUERPERIUM

976. **Factors Influencing the Post-Partum Period and Early Puerperium.** (Om efterbördsskiftet och den tidigare delen av puerperiet samt därpå inverkande faktorer.)

By H. SAURAMO. *Nord. Med.*, 34, 1095–1100, May 9, 1947. 33 refs.

The author has collected a material comprising 2,000 uncomplicated spontaneous deliveries in 1936 and 1945 for the purpose of discovering the factors which may influence the postpartum and puerperal infections. The following observations were made on the basis of this material: (1) Advanced prophylaxis has evidently increased the number of uncomplicated spontaneous deliveries and decreased the incidence of albuminuria-nephropathy. (2) Puerperal infections in spontaneous deliveries have not diminished. (3) Young parturients, and especially primiparae, for whom the deliveries are often strenuous, are particularly liable to puerperal infections. (4) Earlier infections in the genitalia, episiotomies of the second degree, or perineal rupture may increase the number of puerperal infections. (5) An internal examination properly done and rupture of the membranes do not cause an increase of puerperal infections. (6) A prolongation of the postpartum period does not, evidently, reduce the incidence of puerperal infection or retention of parts of the placenta. (7) The duration of the postpartum is longer, on an average. in such cases in which bleeding has been abundant during the postpartum period (atony). (8) If haemorrhage is profuse during or/and after the postpartum period puerperal infections are obviously more frequent.

The following conclusions were drawn: (1) Prophylaxis with respect to mother and child is very important and should be started before pregnancy. (2) The delivery as a whole is not so physiological in Finland as among primitive